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THE CUTANEOUS REACTION OF SYPHILIS.

PRELIMINARY NOTE.

By Julian Mast Wolfsohn, M. S., M. D.,

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Given a case of infectious disease, the first aim of the physician is to make an early and exact diagnosis. In order to do this, recourse to special methods, the difficulties and restrictions of which are beyond the reach of the general practitioner, is often necessary. The Wassermann reaction in syphilis is an instance in point. The desirability of more simple tests, which are at the same time accurate, is at once apparent.

Since the discovery of tuberculin by Koch, a new field in the diagnosis of tuberculosis has been opened. For diagnostic purposes many methods for the administration of tuberculin have been described, among which may be mentioned:

1. The subcutaneous method;
2. The cutaneous method of von Pirquet;
3. The ophthalmo reaction promulgated separately by Wolff-Eisner and by Calmette;
4. The percutaneous reaction of Moro and Goganoff; and
5. The intradermal method of Mantoux and Moussu. This last method, the authors state, is sufficiently sensitive to reveal tuberculosis in domestic animals. Administered in this way tuberculin gives rise to no general disturbance, and it is asserted that it possesses all of the advantages of the subcutaneous method for diagnosis and none of its disadvantages. This method is now being used widely for the diagnosis of human tuberculosis.

Other special diagnostic methods, such as that of complement fixation and that of the opsonic index have been recommended from time to time, but the results have been extremely variable; they seem to be of little value.

Undoubtedly, through the use of tuberculin, great strides have been made in the early diagnosis of tuberculosis, but to devise the methods the causative organism had first to be isolated and cultivated.

Shortly after the results of the tuberculin tests were reported, many workers, including Wolff-Eisner, Didrachi, Neisser, Bruck, and others, attempted, by applying extracts of syphilitic tissues to the skin of syphilitic patients to obtain a specific reaction. The results were discordant. Neisser and Bruck asserted that the method was valueless, inasmuch as a reaction similar to that produced by the syphilitic extract also could be obtained by the employment of a concentrated extract of normal liver.

Fontana,[1] in a comprehensive report, showed the apparent lack of uniformity in results obtained by various authors. He went over the same ground as these authors, controlling the results by Wassermann reactions. He used several other substances which would lend themselves to intradermal reaction in syphilitic subjects, and compared the results with control tests in the non-syphilitic, as for example:

1. Syphilin, which is a glycerine extract of mucous patches, rich in spirochætes;
2. 10% solution of sodium glycocollate in sterile, distilled water.

[1] Dermat. Wchnschr., 1912, No. 3, 119.

3. Lecithin in the form of phosphoplasmin; and
4. Extract of normal guinea-pig's heart.

A positive reaction was indicated by a distinct nodular infiltration. It is interesting to note that of forty syphilitics, 85% showed positive Wassermann reactions, and only 45% developed positive syphilin reactions. Of sixteen non-syphilitics, 12½% gave positive tests. The results did not seem to be influenced by antiluetic treatment.

Using the sodium glycocollate solution in twenty-nine syphilitics he obtained a positive reaction in only 40%, and in fifteen non-syphilitics a negative reaction in all. In twenty-two syphilitics, in which both the Wassermann reaction and the intradermic tests with glycocollate solution were made, 89% showed positive Wassermann reactions, and 27% positive glycocollate solution reactions.

Lecithin injections produced only three positive tests in eighteen luetic cases.

Extract of guinea-pig's heart was used in three patients suffering from syphilis, all of whom gave positive reactions, whereas of ten non-syphilitics only two reacted positively.

The author's conclusions, drawn from this series are, that, "of these substances, syphilin *may* become of some use in the future." Neisser and Bruck early found that the skin of syphilitics late in the disease is in a state of *Umstimmung,* or susceptibility to trauma, and this may readily explain the reaction to the injections of extract of guinea-pig's heart in the skin of syphilitic subjects.

In 1905, Schaudinn established the spirochæte pallida as the causative agent for syphilis. Numerous efforts were made to isolate the organism in culture, but without success. It remained for Noguchi [2] to discover the method of cultivating these organisms, first by the indirect, later by the direct method. He showed that in order to cultivate the pallida directly from the primary lesions in man, two all-important conditions must be fulfilled:

1. The maintenance of strict anærobiosis; and
2. The property possessed by the spirochætes pallida of migrating in solid media in which they are multiplying.

The culture media used consists of:

1. Ascitic fluid containing a piece of sterile placenta; and
2. Ascitic fluid agar, also containing a piece of placenta.

The organisms are grown for 6 to 50 days. After sufficient growth has taken place the tissue is removed, and the solid media and organisms ground in a mortar and diluted with the ascitic fluid culture. The mixture is then heated for 60 minutes at 60° C., and 1% tricresol is added as an antiseptic. Noguchi has called this final sterile emulsion "luetin," and it is this preparation which was used in the tests reported in this paper.

As Noguchi l.c. points out "pure cultures of the treponema pallida offer many advantages, because not only are pallida of different ages present, but also their metabolic products," which, he states, are important factors in establishing an allergic state in syphilitic subjects.

[2] J. Exp. M., 1911, xiv, 99. Idem. 1911, xiv, 556.

Method.

In the following series of cases the method advised by Noguchi has been strictly followed.

Both arms of the patient were cleaned with 95% alcohol; 0.1 cm. of the luetin was injected intradermally into the left arm over the biceps muscle and the same amount of the control emulsion (which consists of the media only and no pallida) was similarly injected into a corresponding site on the right arm.[3] Observations were made daily thereafter over a period of twelve to thirty-six days.

To insure the sterility of the emulsions, cultures from them were frequently made.

Every patient upon whom the luetin test was tried, had a Wassermann reaction done on his blood serum and upon his cerebrospinal fluid, when this was indicated.

Very few reactions presented any difficulty in interpretation, i. e., practically all the reactions were definitely negative or positive.

The Negative Reaction.

In the majority of cases, 24 hours after the injection, the skin in the injected arm showed a slight blush, and a moderate induration or papule formation. Very seldom was any tenderness or itching complained of, which has been only too frequent in the cases showing positive reactions.

Almost invariably, after 48 hours, the injected site would be free from induration and erythema; a pinpoint ecchymosis or perhaps a small yellowish pigmentation alone remained. If the patient has irritated the site of injection a small pustule may form, but this latter has only developed in two of the control cases and has not given rise to confusion in interpretation.

Positive Reaction.

Though the type of reaction in positive cases varies greatly, in general the gross characteristics are induration and erythema. In analysing the various types of reaction found in the different stages of syphilis, the following classification includes all the essential varieties:

(a) *The Papular Form.*—Arising at the site of the injection within 24 hours an indurated papule developes which varies in size from 5 to 15 mm. in diameter and this is surrounded by more or less erythema and is usually quite tender. The reaction gradually increases in size until the 3d or 4th day, when it either regresses or developes into the pustular form. The control injection (in the other arm) in these cases usually shows no reaction after 24 to 48 hours.

(b) *Vesicular Form.*—This variety is generally seen in cases where a moderate reaction rapidly follows the injection, and it occasionally appears as a bleb, but more often as a group of small vesicles superimposed on an indurated, tender base. As a rule, the vesicular passes into the pustular variety.

[3] To correctly perform the intradermic injection, the hypodermic needle, which must be of very fine bore (e. g., the Sub Q syringe needle) is inserted almost parallel to the skin in an effort to reach the under surface of the derma. The bevel on the end of the needle should be turned toward the skin.

(c) *Pustular Form.*—This may be primary or secondary. When primary it occurs usually in association with the violent reactions seen in latent or in late tertiary stages of syphilis where no treatment had been previously administered. When secondary it occurs late in the papular form or developes early from the vesicular stage.

The pustules usually rupture spontaneously with subsequent crust formation.

In a few latent and parasyphilitic cases a week after all evidence of reaction at the site of the injection had subsided a hemorrhagic pustule appeared, which, when opened, exuded a semi-fluid grumous hemorrhagic material.

(d) *Torpid Form.*—Noguchi has aptly so named this variety. It was found that, in many of the parasyphilitics showing vascular luetic lesions, for 3 to 7 and even 28 days following the injections, the reactions were quite negative; but the site of injection, after this period of quiescence, possesses a bluish-red tinge and a smaller or larger indurated papule is felt. This soon increases in size, is not tender, and in the 2 or 3 days following developes into a pustule, after which there is a regression of the reaction. In these cases the control injection site showed nothing abnormal.

In brief, the reactions may be said to be (1) mild, (2) violent, or (3) torpid, according as the signs slowly develop to a maximum and regress; start in violently reaching an early maximum, which is maintained for 24 to 72 hours, and then subsides; or develop late and show only a mild reaction after a latent period and never become marked.

In no case did scar formation follow after local manifestations subsided, but in many instances there was more or less pigmentation, according as the site of injection was markedly hemorrhagic or not.

Non-Syphilitic Cases.

Of the seventy controls in which the patients were suffering from diseases other than syphilis, e. g., soft chancre, mitral insufficiency, myocardial insufficiency, cancer of the tonsil, acute rheumatic fever, pregnancy with still born infant, senile palsy, bronchitis, brain tumor, diabetes mellitus, pleurisy with effusion, pericarditis, hypophysis tumor, pernicious anæmia, epilepsy, peliosis rheumatica, sarcoma of the ileum, myelogenous leukemia, carcinoma of the stomach, thyroid cyst, pulmonary tuberculosis, chronic nephritis, rickets, chronic constipation, gastric ulcer, uræmia, typhoid fever, and infectious arthritis, etc., when no history of syphilitic infection could be obtained and where the Wassermann reaction was negative in each case, no positive luetin or control reactions were obtained. In two cases, small non-indurated pustules developed within three days after the injection, but these easily could be distinguished from the positive reactions. No constitutional symptoms were complained of or noted in these cases.

Primary Syphilis.

No opportunity as yet has been afforded to try this test on patients suffering from primary syphilis.

Secondary Syphilis.

Two cases of secondary syphilis, both in the maculo-papular stage, were inoculated. In each case the Wassermann reaction was positive and each patient had been given 0.4 gram salvarsan intravenously 24 to 48 hours before the test was given. Both tests were positive. In the first case the salvarsan had been administered only 24 hours before, but the reaction to the luetin, although delayed till the fifth day, was definitely positive. No constitutional symptoms or reaction (*Umstimmung*) over the site of injection of the control emulsion were noted.

Tertiary Syphilis.

This series includes six cases in which the Wassermann reaction was positive in five. The sixth patient had had 0.6 gram of salversan one year before admission and his test proved negative both with blood serum and cerebrospinal fluid at this time. The Wassermann reaction was positive in 1911, however. The luetin reaction in this case was positive. In the first case of this series the luetin reaction was negative though the Wassermann was positive. This case was not followed longer than 10 days.

The reaction in four cases of luetic periostitis was of the violent variety and showed early pustule formation and rather marked reaction on the control side (*Umstimmung*). Two of these complained of tender and painful arms and one developed enlargement of the axillary glands. All these manifestations disappeared in 48 hours.

It is interesting to note that, in one case, two weeks after subsidence of the local manifestations there was a flare up at the site of the injection of luetin. A pustule formed and rapidly disappeared, leaving no other signs than slight desquamation and pigmentation.

The rapidity with which the reaction becomes manifest, the ease with which it is interpreted, together with the almost constant development of it, in this stage of the disease makes it a most valuable aid in diagnosis. It not only checks up the Wassermann reaction, but it may be indeed supplementary to it, especially in the treated cases, in which the Wassermann reaction not infrequently may be negative.

Parasyphilis.

If one accepts the newer conception of parasyphilis he will include not only tabes and general paresis, but also those cases which show vascular changes of luetic origin, e. g., cases of syphilitic mesaortitis and aortic aneurysms. Therefore, included in this series are nineteen cases, seven of which are of central nervous system affection, and twelve of cardiovascular disturbance.

A careful analysis of these cases shows the great value of the luetin test. Of the former cases all seven gave positive tests, while the Wassermann test was negative in six.[4] One of

[4] Of course one must keep in mind the limited number of cases that the luetin test has been tried on; the result, however, even in this small series has been striking.

these, a tabetic, had a positive Wassermann reaction one year previously and had had in the interim three doses of salvarsan, but the cerebrospinal fluid still gave a positive Wassermann test. The luetin reaction in this case was violent, the reaction over the site of control injection (*Umstimmung*) being especially noticeable, as it was also in five of these cases.

Another tabetic who showed no other signs than diminished knee kicks and sluggish pupils, developed remarkable constitutional symptoms, beginning 30 hours after inoculation and lasting four days. These symptoms consisted of fever as high as 103° F., pain in the abdomen resembling crises, with nausea and vomiting. The reaction was violent and *Umstimmung* was present. The Wassermann reaction was negative, both for the blood serum and cerebrospinal fluid in this case. This patient had never received treatment previous to this time.

Of the twelve parasyphilitics showing cardiovascular lesions, eleven gave positive luetin reactions and one reacted negatively. Only seven showed positive Wassermann reactions. The one case giving a negative luetin test had a positive Wassermann reaction. But six of this series giving negative Wassermann reactions gave positive luetin tests. It is in this group of cases in which great care must be exercised, as one might readily consider the test negative if it were not watched for some time. Six of these twelve cases showed reactions of the torpid form, no sign of the reaction appearing until the 9th day, and in one case of abdominal aneurysm, which gave a positive Wassermann test, there was no manifestation until the 28th day. The luetin reaction will prove of great value in this type of case, if properly followed, because the Wassermann tests are relatively inconstant. *Umstimmung* is infrequent here as compared with cases of parasyphilis of the central nervous system. No other cases showing constitutional symptoms were noted.

Latent Syphilis.

This stage of syphilis shows a wonderful constancy of results with this test. In the twenty-three cases of latent syphilis tested all gave positive reactions. The Wassermann reaction in this series was positive only in ten cases. In three of these cases the Wassermann reaction with the cerebrospinal fluid was also negative.

Some of the cases reported in this group denied having contracted syphilis, but after the luetin test was found positive, in several instances the patients confessed having had a primary lesion or secondary manifestations. The test was applied in four cases of pregnancy, three of which were terminated by the birth of macerated fœtuses and the fourth by the birth at term of a still born infant. All four patients denied infection. The three former patients reacted "violently" to the luetin and showed *Umstimmung*. The Wassermann reaction was positive and an anatomical diagnosis of syphilis in the infant was made in each case. The fourth case gave a negative luetin reaction, the Wassermann reaction was negative and no signs of syphilis could be discovered in the dead infant. No constitutional disturbances were noted in these cases.

Of the remaining nineteen cases in this series, nine showed *Umstimmung*. One patient suffering from carcinoma of the head of the pancreas, who had a chancre in 1865, showed a delayed luetin test, but gave a negative Wassermann reaction.

Constitutional Symptoms.

Constitutional symptoms consisting of tender axillary glands, tender arms, tachycardia, abdominal pains, bone pains and nausea were present in four of the cases, but these symptoms were usually of only 24 to 48 hours duration and caused no alarming discomfort to the patient. One case showed a secondary hemorrhagic pustule two weeks after the first manifestation had subsided.

Thus, latent syphilis, so difficult to diagnose clinically and in which the Wassermann reaction is not of assistance in over 40% to 70% of the cases, shows a positive luetin reaction in all the cases tried. It seems that the luetin reaction will prove of even greater value in the diagnosis of this group than in the tertiary stage in which the Wassermann reaction is more constantly present. The effects of treatment on the results of the luetin test in latent syphilis has not been significant.

Umstimmung.

In reviewing the whole series of one hundred and fifty cases, another interesting fact was noted—that in many cases of tertiary and of latent syphilis the site of the control injection showed almost as marked a reaction as developed about the point where the luetin was injected. This, as was pointed out by Neisser and Bruck, and which seems to be confirmed by Noguchi and this series of tests, appears to be due to the susceptibility to trauma of the skin of syphilitics late in the disease (*Umstimmung*), for not one of the seventy control patients reacted on the side in which the control emulsion was injected. (Experiments are now under way in which a series of patients, not selected, are being inoculated with the control emulsions only.)

The cases exhibiting the most marked "control" reactions (*Umstimmung*) were those suffering from syphilis in its later stages. The inconstancy of this phenomenon in all probability precludes its being of an allergic nature, which, Noguchi, I believe, has so well shown the principle of the luetin reaction to be.

Conclusions.

1. The luetin reaction is specific for syphilis.
2. The reaction is found of greatest value in the latent and tertiary stages of the disease.
3. In some treated cases of secondary syphilis the reaction is positive.
4. In parasyphilitics with the cardiovascular manifestations of the disease the reaction may be delayed for from 9 to 30 days.
5. The luetin reaction is helpful in the diagnosis of latent syphilis in pregnancy.
6. The state of *Umstimmung* is well brought out in the tertiary and latent forms of syphilis.

SECONDARY SYPHILIS.*

Diagnosis.	Treatment.		Luetin. First day.	Second day.	Third day.	Fourth day.	Later.	Remarks.	Luetin React.	Wassermann.	Constitutional.
Secondary Syphilis (maculo-papular)	"606" 24 hrs. before luetin test given	Lu.	Papule with wide eryth.	Papule; little eryth.	Regression	Eryth. for 1 cm.	Pustule, scab and eryth. in 5, 6, and 7 days	Reaction delayed to 5th day	+	+	Temp. 99.8° F.
		Co.	Small vesicle	No react.	No react.	No react.	No react.				
Secondary syphilis	"606" given 48 hrs. before luetin test	Lu.	Induration and eryth. for 1 cm. *Vesicles*	Many small pustules, eryth. 2½ cm.	Larger erythema, pustules	Large pustules	Pustule ruptured 7th day				
		Co.	Small red nodule	Nodule	.....	.....	.....	.....	+	+	
									2	2	

TERTIARY SYPHILIS.

Diagnosis.	Previous treatment.		Luetin. First day.	Second day.	Third day.	Fourth day.	Later.	Remarks.	Luetin React.	Wassermann reaction. Blood C. S. F.	Constitutional.
Syphilitic cirrhosis of liver; Pulm. tuberculosis.	1896-1899 long irreg. intervals	Lu.	Small nodule	.....	.....	.....	No reaction; slight pigmentation left	.....	Negative	+ Not done	
		Con.	Same								
Syphilitic periostitis	3 months; chancre, secondaries	Lu.	Large indurated papule 5 cm.	Same	Large raised pustule; scab, eryth. regressing	Regression	Flare up 2 wks. later	2 wks. after subsidence of flare up on luetin site pustule *Umstimmung*	+	+ Not done	Enlarged axillary glands
		Con.	Papule and eryth. for 3 cm.	Same	Regression	Scab					
Syphilitic periostitis	None (no hist.)	Lu.	Induration 1 cm.; eryth.	Pustule and eryth. 1.5 cm.	Pustule broke; eryth.	Regression	.....	Pustule *Umstimmung*	+	+ Not done	
		Con.	Same	Large raised papule	Papule and eryth.	Regression					
Syphilitic periostitis *Gummata*	None (no hist.)	Lu.	Vesicles 1 cm.; eryth. slight.	Large irreg. pustule 1.5 cm.	Same	Pustule broke; scab regression.	Regression	Vesicle pustule *Umstimmung*			
		Con.	Small papule	Induration 1 cm.	Pustule formation	Smaller	Regression	.....	++	+ Not done	
Hemiplegia arterio-sclerosis	"606" 1 yr. previously. No hist.	Lu.	Indurated patch	Induration 1½ cm.	Increasing to 2 cm.	Increasing small pustule.	Regression	.....	+		
		Con.	No reaction	No reaction	No reaction	No reaction	No reaction				
Luetic periostitis; polyarthritis	None (no hist.) Miscarriage	Lu.	Induration and diffuse eryth.	Large pustule; eryth. 2.5 cm.	Same	Regression	.....	Pustule	+	+ Not done	Tender arm
		Con.	Small indurated papule	Pustule and eryth. 1.5 cm.	Same	Regression	.....	*Umstimmung*: violent react.	++		
									5 positive 1 negative	5 positive 1 negative	

PARASYPHILIS.

Cerebro-spinal syphilis; beginning dementia paralytica	3 *days*; chancre 1899; iritis 1899	Lu.	Papule and eryth. 2 cm. tender	Pustule; eryth. 3 cm.	Same	Pustule broke	Regression	No scar; on 12th day either side pustule	+	+ +	Tachycardia to 110
		Con.	Papule; slight eryth.	Pustule and eryth.	Pustule same size on left	Same	Regression	*Umstimmung* rapid			
Myocardial insufficiency; aortic insuff.; syphilis (Wass.)	3 weeks; chancre 1887	Lu.	Induration and eryth. 1 cm.	Very slight infiltration	No reaction	No reaction	No reaction	.....	..	+ Not done	
		Con.	No reaction	No reaction							
Transverse myelitis	3-4 months; chancre 1902; secondaries	Lu.	Papule and eryth. 7 mm.	Same	Same	Pustule and infiltration 1.5 cm.	Pustule broke 9th day	.....	+	.. Not done	
		Con.	No reaction	Same	No reaction	No reaction	No reaction				

* In all tables the abreviations indicate as follows:
Lu. = luetin. Con. = control. Eryth. = erythema. C. S. = cerebro-spinal. Wass. = Wassermann. C. S. F. = cerebro-spinal fluid

PARASYPHILIS—*Continued.*

Diagnosis.	Previous treatment.	Luetin.						Remarks.	Luetin React.	Wassermann reaction. Blood	Wassermann reaction. C. S. F.	Constitutional.
			First day.	Second day.	Third day.	Fourth day	Later					
Myocardial insuff.; aortic insuff.	None; secondaries 1911	Lu.	Pustular induration 1½ cm.	Increased reaction	Regression	Regression	Reaction ended	.....	+	..	Not done	
		Con.	Slight eryth. 1 cm.	Same	No reaction	No reaction	No reaction					
Aneurysm aortic arch	None; chancre 1908	Lu.	Small papule	No reaction	No reaction	No reaction	On 11th day area inflam.	Delayed pustule	+	..	Not done	
		Con.	Same	No reaction	No reaction	No reaction						
Myocardial and aortic insuff.	None (no history)	Lu.	Large induration and eryth.	Same	Regression; some eryth. still.	Small pustule broke 6th day	.....	.....	+	..	Not done	
		Con.	Small papule	No reaction	No reaction	No reaction						
Myocardial insuff.	None (no history)	Lu.	Indurated papule; eryth.	2 small vesicles; induration.	2 pustules; eryth. 1 cm.	Same	Vesicles again on 7th day	2 crops of vesicles; pustules	+	20% fixation	Not done	
		Con.	Small papule	No reaction	No reaction	No reaction	No reaction					
Myocardial insuff.	None (no history)	Lu.	Indurated papule 1 cm.	Increased induration and eryth.	Small pustule; induration; same	Went home	Went home	.....	+	+	..	
		Con.	Same	Smaller papule	Regression							
Aortic insuff.	1 year; chancre 1899; secondaries 1899	Lu.	Slight indurated papule and eryth.	Same	No reaction	No reaction	On 9th day much induration and eryth. 2 cm.	Delayed	+	..	Not done	
		Con.	No reaction	No reaction	No reaction	No reaction	No reaction					
Dementia paralytica C. S. Lues	Short while? chancre	Lu.	Induration and eryth.	Induration and eryth. for 2 cm.	Larger induration; pustule	Pustule broke; crust; regression	Regression	Vesicles and pustules; *Unstimmung*	+	..	..	
		Con.	Papule	2 small vesicles; induration	Large infiltration	Pustule	Regression					
Aneurysm of aortic arch; myocardial insuff.; syphilis (Wass.)	None	Lu.	Nodule small	Regression	Regression	Regression	3 weeks later flare up in control; *hemorrhagic*	Delayed *reaction*, 3 weeks' hemorrhagic in luetin side	+	+	Not done	None
		Con.	Nodule small	Regression	Regression	Regression						
Aneurysm of abdominal aorta; syphilis (Wass.)	3 mos. (1890) (primary and secondaries)	Lu.	Nodule small	Regression	Regression	Regression	4 weeks after luetin inj. =eryth. some infiltration *pustule*	*Delayed*	+	+	Not done	None
		Con.	Nodule small	Regression	Regression	Regression		Pustular				
Tabes dorsalis; acromegaly; syphilis (Wass.)	1 mo. 1897; 3 doses "606" 1911-1912; prim. and secondaries	Lu.	Infiltration and eryth. 3 cm.	Vesicles and induration	Large indurated mass with eryth.	Regression	6th day react. over; pigmentat. desquama	*Rapid* react.; vesicles; pustules; both sides react. con. more than luetin	++	+1911 −1912	+1912	None
		Con.	Eryth. and induration 1.5 cm.	Regression	Larger induration pustules	Regression	Same; no scar		+++			
Arterio-sclerosis; aortic insuff.; syphilis (Wass.)	3-4 weeks 1900; prim. and secondaries	Lu.	Induration red area 7 mm.	Increasing area of induration 1.5 cm.	Pustule	Regression scab	No further reaction	Rapid react.	+	+	Not done	None
		Con.	Same as Lu.	Small papule	Less reaction	Small pustule; no induration; no eryth.	Regression					
Myocardial insuff.; aortic insuff.; syphilis (Wass.)	1 week (1899) chancre	Lu.	Small infiltrated papule 5 mm.	Same	Small desquamation; papule	Regression	11th day 2d pustule	*Delayed*	+	+	Not done	None
		Con.	Infiltrated papule 4 mm.	No reaction	No reaction	No reaction	No reaction	Pustule				
Myelitis	None	Lu.	Indurated papule with tenderness 1.5 cm.; eryth.	Small pustule; some induration	Increasing induration and pustule	Same	Pustule broke 6th day	Both sides reacted; control delayed; pustules; *Unstimmung*	+	..	Not done	None
		Con.	Same; less eryth.	Same at 28 hrs.	Small pustule	Fluctuating pustule	Scab					
Tabes dorsalis; chr. nephritis	3 mos. (1897) chancre	Lu.	Large red papule 8 mm.	Small tender pustule; induration for 1.2 cm.	Scab; induration	Regression	4 weeks later 2d induration and pustule foll.	2d *delayed* react. in luetin side	+	+	..	None
		Con.	Small papule	No reaction	No reaction	No reaction	No reaction	*Pustule* formation				

PARASYPHILIS—*Continued.*

Diagnosis.	Previous treatment.		Luetin. First day.	Second day.	Third day.	Fourth day.	Later.	Remarks.	Luetin React.	Wassermann reaction. Blood C. S. F.	Constitutional.
Aneurysm of aortic arch	1 year: chancre 1902	Lu.	Small indurated papule	Small pustule; induration still present.	Same	Small blood crust; less induration	Regression	Mild react.: *pustule*	+	+ Not done	None
		Con.	No reaction	No reaction	No reaction	No reaction	No reaction				
Tabes dorsalis	None (no history)	Lu.	Slight induration; diffuse eryth.	Induration; eryth. for 3 cm. pustule	Large pustule with crusts; eryth. 3 cm.	Same	Regression	Rapidly fulminating case: *pustule* formation	+	.. ..	Fever to 103°F. pain in abdomen; vomiting and nausea beginning 30 hrs. after and lasting 4 days
		Con.	No reaction	Slight induration	Small pustule; little reaction	Same	Regression	*Unstimmung*			
									18 positive 1 negative	10 positive 8 negative 1 C. S. F. positive	

LATENT SYPHILIS.

Acute lobar pneumonia	2 months (chancre 1909)	Lu.	No induration; slight blush.	Indurated papule	Small pustule; eryth. 6 mm.	Large pustule	Not seen	.....	+	.. Not done	
		Con.	Same	No reaction	No reaction	No reaction					
Typhoid fever (?)	1-2 days; secondaries 1900	Lu.	Large eryth. 6 cm.; induration 2 cm.	Few vesicles added	Large infiltrated pustules with erythema.	Confluent pustules	8th day pustule broke	Violent reaction; hemorrhagic after 2 wks.	++	.. ..	Very tender axillary glands 2 weeks
		Con.	Induration and eryth. for 2 cm.	25 small pustules	Regression	Regressing	No reaction	Pustules. *Unstimmung*			
Pulmonary tuberculosis?	1 year constantly (chancre 1911)	Lu.	Induration and eryth.	Large pustules	Pustule broke	Regression	No reaction	Pustule. *Unstimmung*	+	.. Not done	
		Con.	Eryth. 2 cm.	Papule with erythema	Small pustule	Regression	No reaction				
Subacute appendicitis	None (no history)	Lu.	Induration and eryth. for 1 cm.	Several small vesicles with eryth.	Large pustule; eryth. 8 cm.	Pustule broke	Scab	Vesicles pustule	+	.. Not done	
		Con.	Same	Papule	Large papule	Pustule	Regression	*Unstimmung*			
Aortic insufficiency	None (no history)	Lu.	Large induration and eryth.	Same—2 cm.	Same	Regression	Small pustule	.....	+	.. Not done	
		Con.	Small papule	No reaction	No reaction	No reaction	No reaction				
Pregnancy syphilis (Wass.)	None (macerated fœtus)	Lu.	Induration and eryth. 2.5 cm.	Eryth. and few large vesicles.	Regression	Not seen	Not seen	Vesicles; violent reaction	++	+ Not done	
		Con.	Small hard papule	Slight papule	No reaction						
Brain tumor (?) hysteria	6 mos. (chancre 1895)	Lu.	Induration. vesicles, eryth. 3 cm.	Pustules, eryth. and induration 4 cm.	Same	Regressing	Regressing	Vesicles; pustules	++	.. ..	
		Con.	Induration and eryth. 1 cm.	Same	Large button	Regressing	Regressing	*Unstimmung*			
Latent syphilis; "basilar meningitis"	"606" 1911 (chancre 1873)	Lu.	Many small pustules; eryth. 4 cm. induration.	Same	Same	Regressing	React. over 9 days	Pustules *Unstimmung*	+	.. Not done	
		Con.	Pustules and eryth. 3 cm.	Large indurated button	Same	Regressing					
Hysteria (?)	None (no history)	Lu.	Papule with eryth. for 2 cm.	Same	Eryth. and induration persists.	Small pustule broke	Regression	.....	+	.. Not done	
		Con.	Small papule	No reaction	No reaction	No reaction	No reaction				
Rheumatic fever; syphilis (Wass.)	None (no history)	Lu.	Infiltrated button	Infiltration with eryth. 1.2 cm.	Same	Pustule	5-6 days; larger pustule	7th day slight desquamation; nodules more tender; pustules; reaction in both sites; *Unstimmung*	+	.. Not done	Nodules were very tender
		Con.	Smaller button	Small vesicle	Small pustule crust	Regression	Reaction over				

LATENT SYPHILIS—*Continued.*

Diagnosis.	Previous treatment	Luetin.						Remarks.	Luetin React.	Wassermann reaction. Blood C. S. F.	Constitutional.
			First day.	Second day	Third day.	Fourth day.	Later.				
Chronic nephritis	None (no history)	Lu.	Small indurated erythema	Larger nodule; eryth.	Small pustules	Not followed further	.....	Pt. showed signs of old chorido-retinitis both eyes	+	.. Not done	None
		Con.	Small nodule	No reaction	No reaction						
Splenic anemia	None (chancre 1904) (cauterized)	Lu.	Indurated eryth. area 2.5 cm.	Large tender induration; pustule	Pustule broke; scab	Local react. gone	Reaction over 9th day	Pustule *Umstimmung*; rapid reaction	+	.. ..	Tachycardia to 100; abdominal pain over enlarged spleen
		Con.	Small indurated area	Papule with eryth.	Large pustule; eryth.	Pustule broke	Reaction disappeared 11th day				
Post. urethritis; tuberculosis. syphilis (Wass.)	None (no history)	Lu.	Small tender papule	2 small vesicles	Same	Small pustule	10th day 2d pustule and induration	2d induration; pustule	+	+ Not done	None
		Con.	Same	Papule with eryth.	Same	No reaction	No reaction				
Catarrhal jaundice syphilis (Wass.)	None (no history)	Lu.	Induration and eryth. 1 cm.; vesicle.	Pustule with eryth. 1.5 cm.	Pustule and eryth. 2.5 cm.	Increasing induration	Regression	.....	+	+ Not done	None
		Con.	Papule and eryth.	Papule and eryth. 1 cm.	Pustule and eryth. 1 cm.	Many small pustules	Regression				
Hysteria; syphilis (Wass.)	1 year at intervals	Lu.	Induration and eryth. 4 cm.	Vesicular and pustular formation	Same	Regression	12th day all signs gone	Pustule *Umstimmung*	+	+ Not done	Bone pains and nausea 12 hrs. after injection; temp. 99.8° F.
		Con.	Blush 2 cm.	Eryth. 2 cm.	Induration and eryth.	Pustule	Same				
Acute bronchitis; syphilis (Wass.)	None (no history)	Lu.	Induration and eryth. 5 cm.	Induration 7 mm.	Induration 1 cm.	Crust; no induration	Nothing 5th day	.....	+	+ Not done	
		Con.	Small papules	Small eryth. papule	No reaction	No reaction	No reaction				
Pulm. tuberculosis; syphilis (?)	None; no history (patient has old iritis)	Lu.	Induration and eryth. for 2 cm.	Same	Same	Smull pustule with eryth. 1.5 cm.	Pustule broke 7th day	Pustule	+	.. Not done	
		Con.	Small papule	Small eryth. papule	Regression	Regression	No reaction 5th day				
Carcinoma of head of pancreas	None; chancre 1872	Lu.	Small papule	Same	Regression	Increasing	7th day induration 1 cm. pustule 10th day larger.	Delayed hemorrhagic and luetin after pustule	+	.. Not done	
		Con.	Small papule	Same	No reaction	No reaction	No reaction				
Paroxysmal tachycardia; syphilis (Wass.)	None (no history)	Lu.	No induration; eryth. 1 cm.	2 small papules; little eryth.	10 small pustules with eryth.	Pustules coalesced	Regression	.....	+	+ Not done	
		Con.	No reaction	No reaction	No reaction	No reaction	No reaction				
Pregnancy; syphilis (Wass.)	None (macerated fœtus)	Lu.	Induration and eryth. 2.5 cm.	Induration and large pustules.	Larger induration and eryth.	Not followed	.....	Vesicle; pustule; *Umstimmung*	++	+ Not done	
		Con.	Same	Very large button with vesicle	Regression						
Pregnancy; child; syphilis (Wass.)	None (macerated fœtus)	Lu.	Induration and eryth. 2.5 cm.	Increased induration and eryth.	Induration and eryth. for 3 cm.	Not followed	.....	*Umstimmung*	++	.. Not done	
		Con.	More induration than luetin side	Larger reaction	Large button						
Hemiplegia	No history; no treatment	Lu.	Induration and eryth. 1 cm.	Large, red. indurated papule 1 cm.	Same	Same; slight regression	Regression	*Umstimmung*	+	.. Not done	
		Con.	Small infiltrated papule	Same	Same	Regressing	Regression				
Carcinoma of jaw	Treatment 1 mo. for 10 yrs. (chancre 1902)	Lu.	Indurated papule; little eryth.	Same	Small hard papule	Same	Small crust 6th day	.....	+	+ Not done	
		Con.	Slight papule	No reaction	No reaction	No reaction	No reaction				

STUDIES IN TUBERCULOSIS.*

By GERALD B. WEBB, M. D., Colorado Springs, Colo.

VACCINATION.

It gives me unusual pleasure to relate to you to-night the investigations we have been making in the West in tuberculosis, for most of the laboratory work has been carried out by two of your own men, Dr. William Whitridge Williams and Dr. George Burton Gilbert, and I am most grateful to them for their assistance.

In spite of improved hygienic conditions every individual is exposed at some time to virulent tubercle bacilli. Hygiene, whenever tried alone without vaccination, has always failed to stop small-pox, and Professor Karl Pearson [1] has recently written, in summarizing the results gained by hygiene and education against tuberculosis, "The relative number of deaths from phthisis has not been diminished by the campaign against the tubercle bacillus, although the absolute number has fallen, but at a sensibly retarded rate."† By means of the skin tuberculin tests it has been shown that in many communities almost every child by the age of puberty has become infected. The present interpretation of this infection allows us to consider that it is nature's crude method of vaccination; the child which survives is placed in a hypersusceptible condition in regard to the tubercle bacillus; the organism possesses now the power of safe defence against small numbers of tubercle bacilli, yet against large numbers the infected organism is more helpless than the non-infected. The condition is one similar to anaphylaxis.

This infection may remain during the whole life of the individual—it would seem to be kept in better abeyence during childhood—but at any time it may lead to destruction of the host through escape of large numbers of bacilli from within, as well as from new massive infection from without.

That in spite of all care generations will continue to become infected would seem to be assured by the recognition of the small numbers of bacilli necessary to cause infection. We have ascertained that from virulent cultures inoculated subcutaneously twenty-five bacilli of the human type infected a guinea pig, seventy-five bacilli of bovine type infected a rabbit, and one thousand infected a calf. We have not yet determined the exact number of human tubercle bacilli that will infect a Rhesus monkey, yet the work we have done would indicate that a few hundred would suffice, and we may presume that children become infected by a similar small number.

Since civilization necessitates this exposure to living tubercle bacilli, the numbers and virulence of which cannot be controlled, and also since these bacteria attack especially vulnerable tissues with the unsatisfactory condition of infection just described, the question at once arises whether, if we could control the numbers, virulence, and point of attack before Nature infects us, we might not possess a form of vaccination which should protect us.

Attempts at the production of immunity to tuberculosis by means of inoculation of dead tubercle bacilli or their products have so far not on the whole been satisfactory. This failure may perhaps be explained in several ways.

The inoculation of the bacillary products may have resulted in an anaphylactic condition of the animal experimented upon, or the subsequent tests for immunity may have been made with too overwhelming numbers of living tubercle bacilli.

The most recent work in this country in the attempt to produce immunity by means of dead products of tubercle bacilli is that of Krause [2] of Saranac (N. Y.) and Meakins [3] of Montreal (Can.). By the use of a watery extract Krause found that the more frequently he inoculated the more hypersensitive the guinea pigs became. In testing the immunity by a subsequent inoculation of a small dose of living tubercle bacilli he found that in general the more protein the animal received during preliminary treatment the less the resultant infection.

Meakins used inoculations of an emulsion of dead tubercle bacilli and found that if given in sufficient amounts over a long enough period he produced an active immunity to virulent tubercle bacilli. He found these inoculations increased very markedly the phagocytic power of the blood. He suggests that the injection of killed tubercle bacilli might be taken advantage of to produce an immunity in infants before they become primarily infected with tuberculosis. The question at once arises in considering this dosage of tuberculo-protein whether the animals do not become hypersensitive.

I am somewhat inclined to believe with Koch that in the production of immunity to tuberculosis "We shall never obtain better results with non-living bacilli."

It was natural that the application of the living tubercle virus for the production of immunity should have been attempted in cattle. The results, however, of the inoculations of living human tubercle bacilli for the production of bovine immunity have not proven satisfactory. This failure may probably be in part ascribed to the fact that the cattle become hypersensitive, as for some time after the inoculations they may react to tuberculin; in other words true immunity has not been evoked.

In the recently published volume of the Bureau of Animal Industry the following conclusions are reached by the investigators Schroeder, Cotton, Mohler and Washburn:

"Though results have been obtained which are very encouraging to the investigators and which prompt them to strive onward with renewed vigor and hope, no system of bovo-vaccination has reached a stage at the present time that justifies its use in common practice."

The recorded experiments of the British Royal Commission on tuberculosis go to prove the importance of dosage in the transmission of tuberculosis.

* Paper read at a meeting of The Lænnec, a society for the study of tuberculosis, The Johns Hopkins Hospital, March 25, 1912.

† This is probably not so true of New York City where more active preventive measures have been adopted, resulting in a more rapid fall in the tuberculous death rate than in any great city.

We inoculated subcutaneously three full-grown male guinea pigs with thirty-five, seventy-five and one hundred and twenty-five virulent human tubercle bacilli respectively. The inoculations were made in the nipple area and it was possible to follow the course and degree of infection in the inguinal glands. The largest number produced the most rapid infection and in this pig tubercle bacilli were obtained by puncture of the neighboring inguinal glands after three weeks, and the animal was then killed and showed extensive visceral lesions. Tubercle bacilli could not be obtained from the guinea pig receiving thirty-five until the animal was killed six weeks later, and then the disease was strictly limited to the inguinal glands. The lesions in the guinea pig receiving seventy-five bacilli were intermediate in degree to the other two pigs.

The probability is that in infection from dust by inhalation we do not receive very large numbers—at least not millions—of bacilli, probably only a few hundred or less. Infection by the intestinal route requires a much larger number in all experiments than infection by inhalation. Tuberculosis is peculiarly a disease in which both the virulence of the bacteria as well as the numbers received determine the course of infection, and the latter factor may to a certain degree possibly outweigh the former.

Probably a third and important factor is the frequency of dosage. It is recognised that constant contact with the careless consumptive is the cause of some of the most serious infections, and the experience of Lieb with the subcutaneous inoculations of virulent bovine bacilli in rabbits later referred to, would seem to be a laboratory imitation of this condition.

It occurred to me nearly six years ago, after watching the ingenious technic of Professor M. A. Barber,[4] by which he was able to isolate single bacteria, that could we apply this mechanical principle and inoculate animals with increasing numbers of virulent bacteria, beginning with one, we might be able to produce successful immunity. We[5] first worked with mice and anthrax bacilli. It was known that one twenty-millionth of a drop of anthrax broth culture would kill a mouse in twenty-four hours. By inoculating first one bacillus and gradually increasing the numbers we were safely able to give mice doses which inoculated all at one time meant certain death.

Barber[6] followed this work out further, but found that with such a virulent organism as the anthrax bacillus and such a susceptible animal as the mouse much immunity could not be procured.

We[7] next inoculated in a similar manner guinea pigs with virulent human tubercle bacilli. We found that about twenty-five virulent human tubercle bacilli injected subcutaneously in one dose, would often prove fatal to an adult guinea pig.

In one animal we continued the inoculations at weekly intervals for nine months and in all injected safely about one hundred and fifty thousand virulent human tubercle bacilli. This pig was killed and no tuberculosis was found. Portions of its organs and lymph glands were injected into another pig and failed to produce tuberculosis.

Lieb,[8] working in our laboratory, carried on similar work on rabbits with the bovine tubercle bacillus. He was able, by this method, to begin inoculating a litter of rabbits at the moment of birth and to continue the inoculation with safety as they grew.

His work showed that by inoculating increasing numbers of living virulent bovine bacilli there was evidence of immunity production in both young and adult rabbits. Such immunity apparently depended both upon the age of the rabbit and the size of the increasing doses.

For instance Lieb found that in rabbits two weeks old he could safely inoculate at weekly intervals beginning with one bacillus and increasing by the ratio 2, 4, 6, 8, 10, 12; yet should the sequence be 1, 5, 10, 15, 20, etc., tuberculosis was produced. When, however, the rabbits were ten weeks old they could submit to the latter series of inoculations without infection. It was of special interest that in one of his experiments a rabbit receiving a dosage of 1, 25, 50, 100, 200, etc., bacilli died sooner than another of the same litter receiving 1/10 cc. of a thick emulsion of the same culture, evidently the result of an acquired hypersusceptibility.

In the spring of 1910 we[9] carried the work a step farther by inoculating some twelve monkeys (*Macacus rhesus*) with virulent human tubercle bacilli.

The animals were thoroughly tested with tuberculin and shown to be uninfected before the experiments began. Thirty-five bacilli of the culture of human bacilli employed, produced tuberculosis following subcutaneous injection into a guinea pig.

The inoculations * were kept up at weekly intervals over a year, and up to date, after two years, the animals are perfectly healthy. Two of the monkeys received enough virulent tubercle bacilli to kill over ten thousand guinea pigs, and yet these monkeys weighed only as much as three full-grown guinea pigs. The monkeys have been repeatedly tested with tuberculin during the course and none have reacted except as mentioned below.

Six monkeys have been killed and a thorough search has revealed no trace of tuberculous disease. To make no mistake, due to overlooking possible foci of disease, pieces of the different organs and lymphoid glands of three of the animals were injected into guinea pigs and no infection of these was produced.

We have not yet learned the lowest possible number of virulent human tubercle bacilli which will infect a young monkey.

* The following plan indicates how each animal was treated:

1. Control.
2. 25 bacilli in one dose and no further inoculations.
3. 100 bacilli in one dose and no further inoculations.
4. 200 bacilli in one dose and no further inoculations.
5. Increase slowly, 1, 3, 5, 10, 15, 20 bacilli, etc.
6. Increase slowly.
7. Increase rapidly, 1, 5, 10, 20, 50, 100 bacilli, etc.
8. Increase rapidly.
9. Increase slowly, 5, 10, 15, 20, 25, 30 bacilli, etc.
10. Increase rapidly, 5, 15, 45, 75, 125, 200 bacilli, etc.
11. Control.
12. 50 bacilli at one dose and no further inoculations.

We were surprised, however, to find the resistance of monkeys to the culture we employed very much greater than that of guinea pigs. Two hundred and fifty as a single initial dose failed to give one monkey tuberculosis, whereas thirty-five infected a guinea pig.

In testing the monkeys for possible tuberculous infection the conjunctival and intradermal methods were employed.

For the intradermal test one twentieth of a milligram old tuberculin was injected and the skin fold measured according to Römer's directions. In the third test of this kind, by mistake 20 milligrams were injected, with the result that monkeys Nos. 8, 10, and 11 gave reactions.

Monkey No. 11, a control, was immediately killed, but no trace of tuberculosis could be found. The products resulting from maceration of various lymph glands, portions of lungs, liver, spleen and kidneys, were injected into a guinea pig, but no tuberculosis resulted.

We felt, therefore, that the positive skin reaction resulted from tuberculo-protein sensitization.

As a final test we followed the work of White and Fox[20] of Philadelphia and, having kept temperature records for several successive days at 3 p. m., injected 5 milligrams old tuberculin.

The temperature was to be taken every three hours over a period of two days, but in no monkey was there a rise. Monkey No. 1., a control, alone gave the typical night drop subsequent to the injection. The temperature of monkey No. 2, at the end of the 48 hours, kept significantly low. The monkey appeared very sick and we thought he would die. He recovered the next day, but we thought it best to kill him. A thorough search using every means to reveal tubercle bacilli, and also the injection of macerated extract of various organs into a guinea pig, failed to give evidence of any tuberculosis having existed. We therefore concluded that this phenomenon must have depended upon tuberculo-protein sensitization.

In general there seems to have been a suggestion of interference in the normal night temperature drop. This may be due to tuberculo-protein sensitization or possibly to the presence of antibodies resulting from the inoculation of the living bacilli. I am inclined to the latter view, because monkey No. 1, which had received successive tuberculin injections in the tests, just as the others had done, showed no change in the night drop of temperature.

From time to time we have made differential blood counts. In all the lymphocyte percentage has kept high, and this fact has been of some value to show that no infection has taken place.

To attempt the same experiments on children would be cause for grave anxiety. We have shown that such inoculations were harmless and even of some benefit to tuberculous individuals, but this was entirely a different matter from inoculating the non-infected.

A most unusual opportunity, however, was offered by a distinguished scientist dying of tuberculosis, who requested me to inoculate his two children, aged nine months and three years, in a similar manner to that by which we had succeeded with the monkeys—experiments which this gentleman watched with great interest. The children were inoculated with bacilli from a culture of which 150 infected a guinea pig as indicated by the following figures:

NUMBER OF BACILLI INJECTED.

Date	No. bacilli	Date	No. bacilli	Date	No. bacilli
10/20/10	1	11/25/10	18	12/29/10	100
10/27/10	3	12/ 1/10	25	1/ 5/11	125
11/ 3/10	5	12/ 8/10	35	1/12/11	150
11/10/10	8	12/15/10	50		
11/17/10	13	12/22/10	75		

Total number bacilli received by each child, 607.

The following children have been inoculated as the table indicates. The culture used, however, weakened in virulence and we have not ascertained yet the exact number to cause infection in a guinea pig.

The mother of these children, it may be mentioned, was also found to be actively tuberculous. The children were first tested by means of the von Pirquet skin tuberculin test and reactions were found to be negative. The inoculations were started with one bacillus and increased at weekly intervals until six hundred had been injected. The von Pirquet tests were again applied and found negative and some months after the inoculations of the live germs had ceased were once more found negative.

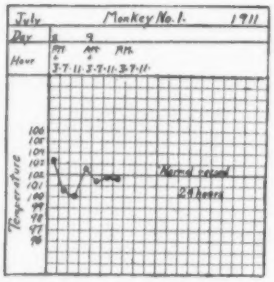
All were tested by skin tuberculin reaction 3/16/12, and all were negative.

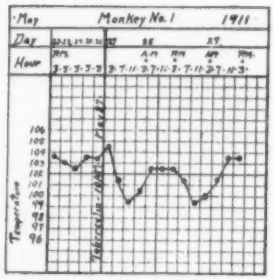
Children.	Age.	Date. 8/29.	8/31.	9/9.	9/18.	9/24.	9/30.	10/7.	10/14.	12/7.	12/14.	12/22.	12/28.	1/4.	1/11.	1/18.	1/22.	1/29.	2/5.	2/12.	2/19.	2/26.	3/4.	9/11.
L.	4 mos.	..	..	..	..	..	..	..	..	1	5	10	15	20	25	35	50	75	100	125	150	200	250	300
V.	6 yrs.	2	4	6	10	15	20	30	40	..	..	..	..	..	..	..	15	25	35	45	65	100	125	150
G.	4½ yrs.	1	2	5	8	12	15	26	35	..	..	..	..	..	..	..	15	25	35	45	65	100	125	150
R.	3 yrs.	1	1	4	8	12	15	24	30	..	..	..	..	..	..	..	15	25	35	45	65	100	125	150
EL.	2 mos.	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	5	8	12	25	35	45	55

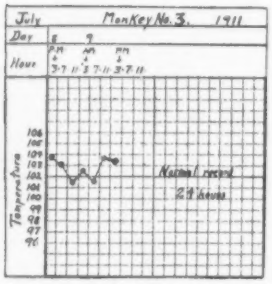
It may be conjectured that in view of a certain degree of racial immunity in man greater than in the monkey, probably a larger number of tubercle bacilli may be needed to infect a child than a monkey. We have, however, not considered this possibility but have inoculated the children with more cautiously graded numbers than we did the monkeys and with a less virulent culture. We may in time learn that perhaps a single dose of a few hundred bacilli inoculated subcutaneously will protect our children, but for the present it is most important to be unusually cautious, and regard the possibility that children can be infected as easily even as guinea pigs.

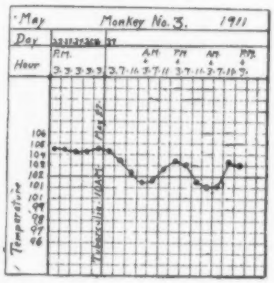
The question as to whether the subcutaneous inoculations will provoke an immunity which will protect the lungs we will work out further in the monkeys. It has been shown, however, that an infected guinea pig will resist a second infection of moderate degree just as well by the lungs as by the subcutaneous tissues. It would seem very necessary to begin such vaccination at birth, whilst the infant is being nursed by the mother.

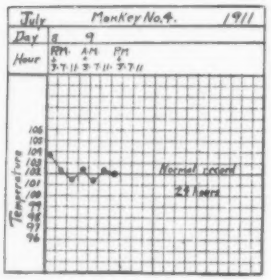
It is possible in hydrophobia to succeed in producing immunization after infection, on account of the long incubation period of this disease. This can hardly be possible in children in

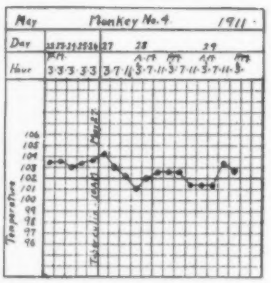

July Monkey No. 1. 1911
Normal record 24 hours
Temperature

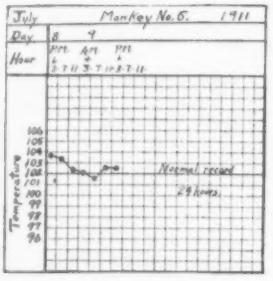

May Monkey No. 1 1911
Tuberculin 1/20 c.c. Daily
Temperature

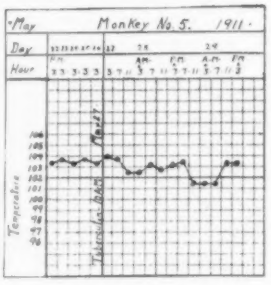

July Monkey No. 3. 1911
Normal record 24 hours
Temperature

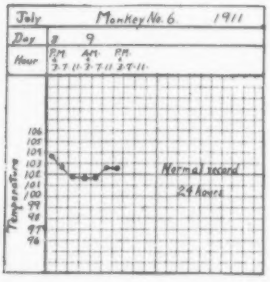

May Monkey No. 3. 1911
Tuberculin 1/20 c.c. Daily
Temperature

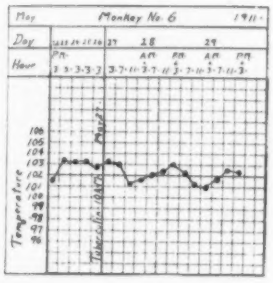

July Monkey No. 4. 1911
Normal record 24 hours
Temperature

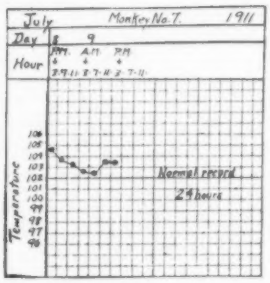

May Monkey No. 4 1911
Tuberculin 1/20 c.c. Daily
Temperature

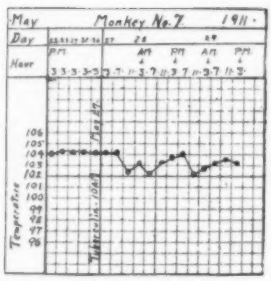

July Monkey No. 5. 1911
Normal record 24 hours
Temperature


May Monkey No. 5. 1911
Tuberculin 1/20 c.c. Daily
Temperature


July Monkey No. 6 1911
Normal record 24 hours
Temperature


May Monkey No. 6 1911
Tuberculin 1/20 c.c. Daily
Temperature


July Monkey No. 7. 1911
Normal record 24 hours
Temperature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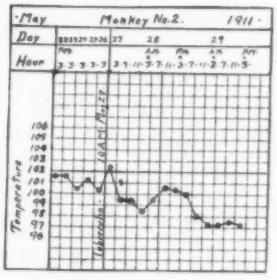
Tuberculin 1/20 c.c. Daily
Temperature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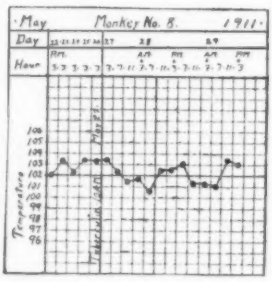
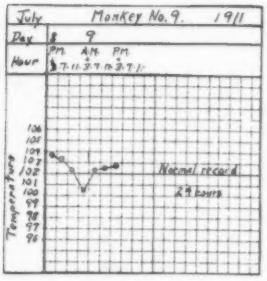
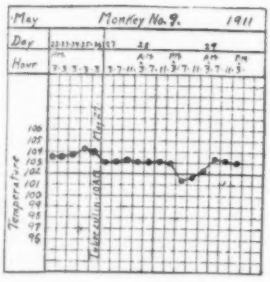
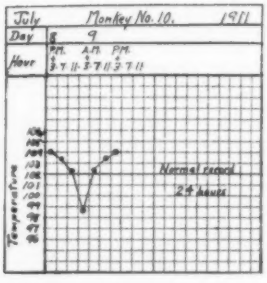
Tuberculin 1/20 c.c. Daily
Temperature


May Monkey No. 8. 1911
Tuberculin 1/20 c.c. Daily
Temperature


July Monkey No. 9. 1911
Normal record 24 hours
Temperature


May Monkey No. 9. 1911
Tuberculin 1/20 c.c. Daily
Temperature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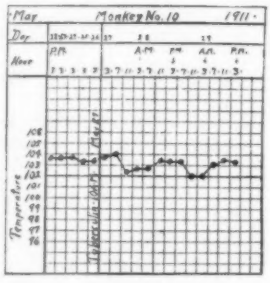
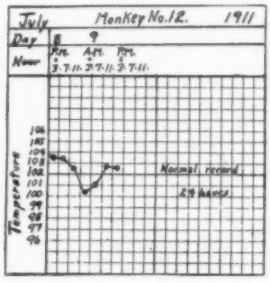
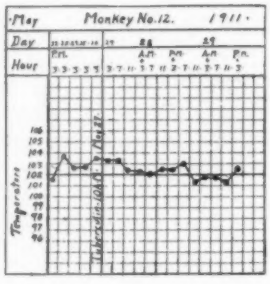
Normal record 24 hours
Temperature


May Monkey No. 10 1911
Tuberculin 1/20 c.c. Daily
Temperature


July Monkey No. 12. 1911
Normal record 24 hours
Temperature


May Monkey No. 12. 1911
Tuberculin 1/20 c.c. Daily
Temperature

tuberculosis for we have found one thousand virulent bovine bacilli infect calves in less than a month so that it would seem better to err in beginning too early, and in children born to tuberculous parents to remove them at birth whilst the vaccination proceeds.

Metchnikoff, in his book "Immunity and Infective Diseases," quotes Massart as saying, "vaccination effects an education of the leucocytes; these latter become so adapted that they can approach the virulent micro-organisms." He goes on to say later that "The acquisition of immunity against micro-organisms is, therefore, due not only to the change from negative to positive chemotaxis, but also to the perfecting of the phagocytic and digestive powers of the leucocytes." He quotes the work of Delezenne in which he proved the phagocytes of a dog could be educated to digest more and more gelatine, when at first they digested it but feebly. This indicates an acquired digestive power. Such acquired digestive power would seem to be most necessary in the defence against tuberculosis.

All our inoculations have been made subcutaneously and the work related would appear to refute Koch's positive statement that "We shall not succeed in habituating the organism to absorbing entire bacilli which have been injected subcutaneously; and by injecting small quantities of them we shall not habituate the organism to absorbing more."

We found for instance in the series of inoculations referred to that when we reached 3000 to 5000 bacilli almost invariably a lump occurred at the inoculation site which would take from one to three weeks to disappear.

This occurrence coincides with the statement of Metchnikoff that "In vaccinated animals the local reaction (in such diseases as anthrax, streptococcus infections, etc.) is more marked, and the exudation very rich in leucocytes. The destruction of the micro-organism, inside these cells, takes a longer or shorter time according to circumstances; but in the end it is always complete."

Following these experiments we tested the monkeys for the presence of antibodies. Emery's [11] method of measuring quantitatively the specific antibodies in a given serum was made use of, but failed to demonstrate their presence. Antibodies were also tested for by means of the meiostagmin reaction described by Ascoli [12] and Izar.[13] None were demonstrated. The phagocytic index which was devised by Neufeld [14] and Hune and Klein and advocated by Meakins [15] seemed to indicate an increased phagocytic immunity in monkey No. 7.

It would seem necessary to recognise two forms of immunity in tuberculosis, the apparent immunity of the infected to reinfection indicated by the phenomenon of Koch, and what may be termed true immunity. In the latter no tuberculin reaction could be expected and it would appear to be the ideal form of immunity to be sought.

It is this form of immunity therefore that we have hoped to attain by this method of inoculation and we believe that this has been achieved.

We have had some forty volunteers for treatment with inoculations of living tubercle bacilli. The procedure has been similar to that reported for the production of immunity. We have not inoculated beyond 5000 bacteria. In general the patients have been in the Turban III class. The results will be given in detail at another time, but it can be stated now that some good would seem to have been accomplished and never has harm resulted. We feel that perhaps better results would appear from larger doses. The future might indicate the necessity for enough bacilli to be inoculated subcutaneously to produce a local lesion. It is well known that a local lesion in some part of the body is frequently of much benefit to tuberculous lung processes.

White Blood Cells.

The defense of the organism against the tubercle bacillus has in general been ascribed to the tissue cells rather than to the white corpuscle. From our own work in studying the white corpuscles of patients with pulmonary tuberculosis we feel we can thoroughly agree with the reported work of Craig [16] of Philadelphia, who finds that the earlier the stage of pulmonary tuberculosis the fewer are the leucocytes, but the earlier the stage the more numerous are the lymphocytes and mononuclears, and the fewer are the polymorphonuclears.

We have shown that the differential blood picture is of some value in indicating the presence of tuberculosis and also its prognosis, as the following chart will testify:

CURED CASES OF PULMONARY TUBERCULOSIS.
57 cases; 100 counts.

Polymorphonuclears	Mononuclears			Eosinophiles	Mast-cells
	Average	Mean	Extremes		
55.5	41.7	41	25-63	2.3	0.5
IMPROVING CASES. 43 cases; 114 counts.					
5.49	38.5	37	18-54	1.7	0.4
STATIONARY CASES. 44 cases; 125 counts.					
63.6	34.4	33	18-50	1.6	0.4
CASES PROGRESSING UNFAVORABLY. 43 cases; 150 counts.					
70.8	27.5	27	14-46	1.3	0.4

In following the later work on immunity investigations in tuberculosis, one is struck with the growing importance placed upon the lymphocytic element as the chief machinery of the organism's defense. Bartel [17] states that the behavior of tubercle bacilli that have entered the body through natural channels indicates a protective action on the part of the cells of organs, and especially of lymphocytes, against infection.

Recent researches by Opie [18] show that the epithelioid cells in tuberculous tissue contain an enzyme exactly similar to that possessed by the large mononuclear leucocytes of the circulating blood. His work indicates that these epithelioid cells may in reality be emigrated large mononuclear leucocytes, which they very closely resemble.

Nichols [19] has shown in the histological study of the lesions of immunized rabbits that the reaction to infection on the part of the lung of the vaccinated animals is much more rapid and intense than in the control or non-vaccinated animals. He intimates that the tissue cells could hardly multiply quickly enough to account for the excess of epithelioid cells, and that more probably most of these are leucocytes from the blood.

The participation of the lymphoid cells in tubercle formation has long been known, and Metchnikoff has claimed the giant-cells to be accumulated macrophages. In experimental tuberculosis the response of tissue to a beginning infection is accompanied by an accumulation of polymorphonuclear leucocytes, but these are soon deplaced by epithelioid and lymphoid cells.

Claude and Zaky [20] in 1902 showed in animals which best resisted tuberculous infection the presence of many large mononuclears. Halbron [21] in 1903 also emphasized the importance of these cells. In 1905 Ullom and Craig, in summarizing their investigations on blood studies in pulmonary tuberculosis, stated that they had received the impression that the actual increase in the lymphocytes corresponded to increased resistance of the patient to tuberculosis. It is also an interesting fact that the age period of greatest outbreak of pulmonary tuberculosis, is not that of childhood, when the percentage of lymphocytes is greatest.

In addition to the evidence given as to the defensive behavior of lymphocytes, Daels [22] has shown that the von Pirquet skin reaction to tuberculin is characterized by the collection of lymphoid cells at the irritated area. Josué [23] shows that in localized experimental tuberculosis in rabbits the bone-marrow responds to infection by a very intense proliferation of the mononuclear leucocytes, and also that the subcutaneous injection of tuberculin will bring about similar marrow activity.

Cadbury [24] found in patients dying of pulmonary tuberculosis that if the bone-marrow was found proliferated, it was practically the rule to find a considerable number of lymphocytes.

It is especially noteworthy that two years ago Bergel [25] in Germany, and Marie and Fiessinger [26] in France, made the important discovery that the lymphocytes contain a ferment of lipolytic power capable of splitting wax and fax into glycerin and fatty acids. Following Opie's method of nomenclature, we suggested for this ferment the name of lympholipase. It has long been known that at least 30 per cent by weight of the body of the tubercle bacillus is composed of waxy substances, and the chronicity of tuberculosis has been thought to be due to the difficulty the defensive mechanism of the host must have to destroy this waxy substance. It is possible too that the polymorphonuclear cell contains some lipase. We were able to corroborate Bergel's observation by finding that pus from a cold abscess digested the surface of beeswax on which it was placed.

Pribram [27] believes in a lipolytic ferment being present in the blood, but does not feel sure, on account of his failure in a small number of experiments, that it is yet completely proved that lipase originates in the lymphocytes.

We have ourselves studied the lysis of tubercle bacilli by the lymphocytes of cockroaches and grasshoppers. These insects would seem to have entirely this type of cell, corresponding to our large lymphocytes. Injections of tubercle bacilli can readily be made into one hind leg, and at various intervals lymphocytes containing tubercle bacilli in all stages of digestion can be found by withdrawing some circulating fluid from the other hind leg.

We have been struck by the length of time necessary for this digestion, often several days and not several hours only, as might be thought.

Fiessinger [28] has published a paper on the part played by lipase in the defense against tuberculosis. Plates accompanying his paper illustrate the lysis of tubercle bacilli by the lymphocytes of the bee-moth larva.

Fiessinger concludes that the lymphocytes furnish lipase, which destroys the waxy parts of the tubercle bacillus, and that it is then necessary for the polymorphonuclear leucocytes to appear with their leucoprotease, which only works in an alkaline medium, to complete the digestion. He would seem to overlook the fact that the lympholipase, by splitting wax into fatty acid and glycerin, might supply the acid medium in which the lymphoprotease could act.

Then, too, we know that complete lysis can proceed in insects which have no polymorphonuclear leucocytes, but only lymphocytes.

It has been shown by Opie [29] that the injection of living leucocytes, consisting of an approximately equal suspension of polymorphonuclear and of mononuclear cells obtained from normal dogs and injected into dogs which have been artificially infected with the tubercle bacillus, can inhibit the development of tuberculous lesions. This would seem to show the value of increasing the numbers of leucocytes.

Manwaring [30] has recently shown that subdural inoculations of tubercle bacilli in dogs produce meningitis. A suspension of leucocytes procured from another dog injected subdurally delays the progress of the disease and prolongs life.

During an epidemic of whooping-cough in the fall of 1908 we attempted to diagnose this disease from an epidemic of catarrhal bronchitis by means of differential leucocyte counts. Barach [31] in July 1908 had recalled attention to the increased percentage of lymphocytes which characterized pertussis, and showed the value of differential counts in establishing a diagnosis. He found both a leucocytosis and a lymphocytosis. The smaller lymphocytes first increased, and the large lymphocytes followed the course of the small ones, reaching their greatest numbers, however, after the small lymphocytes had reached theirs.

After investigating several patients who presented high lymphocyte counts, and yet who clinically we felt certain had only a *micrococcus catarrhalis* infection, we were led to examine the blood of normal children of ages from six to twelve, and found the percentage of lymphocytes higher in all than the normal for sea level.

It happened that at the same time some experimental work

was undertaken on rabbits to ascertain what blood changes, if any, could be brought about by inoculations of mercury, and in the light of the growing importance placed upon lymphocytes in the problem of immunity to tuberculosis, especial attention was paid to see if these elements could be increased.

The result of differential counts on normal rabbits showed that they, too, had a higher percentage of non-granular mononuclear cells than sea-level rabbits, as the following figures indicate:

	Polymorphonuclears	Mononuclears	Eosinophiles	Mast-cells
CHILDREN.				
Colorado Springs.	37.3	60.3	2.0	0.4
Sea Level.....	53	46	1.0	0.0
ADULTS.				
Colorado Springs.	54	43.6	2.0	0.4
Sea Level	61.7	37.4	0.9	0.0
RABBITS.				
Colorado Springs.	31	65	0	4
Sea Level.....	45	52	0	5
GUINEA PIGS.				
Colorado Springs.	19	81	0	0
Sea Level.....	60	40	0	0
MONKEYS (*Macacus Rhesus*).				
Colorado Springs.	31	65.9	1	0
Sea Level*.....	40	55	4	1

* From Hektoen's "Experimental Measles in Monkeys."

The above chart is compiled from a large number of counts. The specimens were taken usually about noon.

It is notorious that observations on white blood cells in regard to both numbers and characters are open to wide variations.

It is recognised that many factors such as sleep, digestion, exercise or time of day render exact comparisons between white cell counts very treacherous, and in addition the techniques for both total white cell counts and differential percentage estimations are also open to not inconsiderable error.

The explanation of the different normals given by various authorities probably lies in these difficulties for exact determinations and comparisons.

Levaditi [32] gives the normal white blood cells per cmm. in healthy adults as 7000-8000, whereas Kjer-Petersen [33] claims 4000-5000 as correct.

The differential white cell picture is according to

	Polymorphonuclears.	Lymphocytes and large mononuclears.	Transitionals.	Eosinophiles.	Mast cells.
Jolly [34] 61.7		35.2	2.2	0.9	
Ehrlich [35] 71		23.5	2	3	0.5

Bunting, of Madison, Wisconsin, has recently published a paper calling attention to the percentage of the different kinds of leucocytes quoted in the literature and making comparisons with his findings at Madison. He suggests that the difference may be due to the fact that in the employment of Ehrlich's original stain some of the lymphocytes did not show up, as they do with the modern Wright stain. Bunting's work, however, was carried out at an altitude of about one thousand feet and his twenty-five reported cases averaging 42% lymphocytes were healthy young adults, mostly students. The following chart is prepared from differential blood counts made from students at Colorado Springs and Harvard.

STUDENTS, HARVARD.
18 cases; 18 counts.

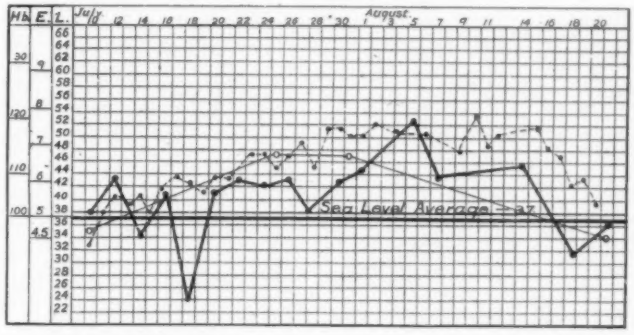
Polymorphonuclears	Mononuclears			Eosinophiles	Mast-cells
	Average	Mean	Extremes		
59.5	38	37	27-56	2	0.5

STUDENTS, COLORADO COLLEGE.
18 cases; 18 counts.

48.5	49.5	52	37-66	1.7	0.3

The following charts are prepared from blood examinations made on Haldane and Douglas of Oxford, Henderson of Yale and Schneider of Colorado College during the recent expedi-

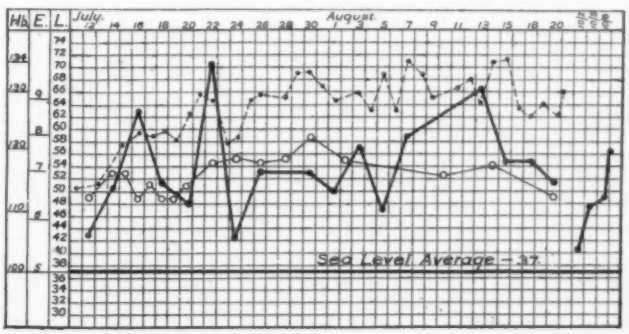
PIKE'S PEAK, 14,000 FT. J. S. H. 1911.
Expedition on Peak lasted from July 12 to August 16.



Hæmoglobin, Hb.
Red Cells, E.
Lymphocytes, L.

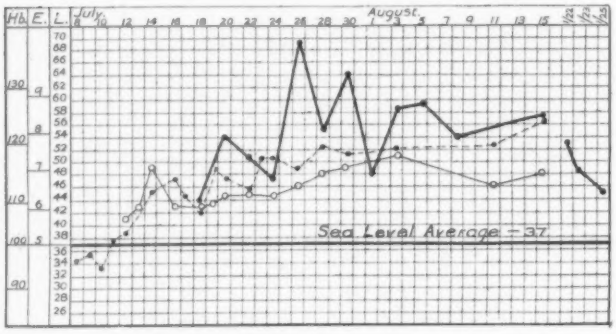
J. S. H. was suffering from a chronic infection and had constantly 15,000 white blood corpuscles.

PIKE'S PEAK. Y. H. 1911.

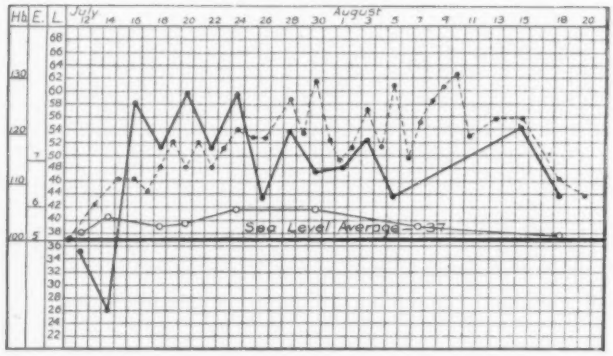


tion to be summit of Pike's Peak, Colorado, for the study of mountain sickness.*

PIKE'S PEAK. E. C. S. 1911.



PIKE'S PEAK. C. G. D. 1911.



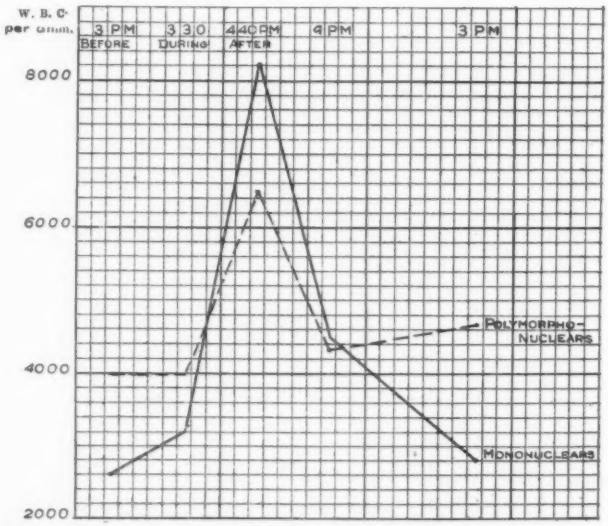
In Charts 2 and 3 the red blood corpuscles indicate an early initial rise and then decline; later, an overproduction. Charts 2, 3 and 4 indicate the overproduction, later referred to, of lymphocytes after 2 weeks.

Zuntz* explains the increased numbers of erythrocytes in high altitudes as due to hyperplasia of the bone-marrow, and by his experiments on dogs, it would seem, conclusively demonstrates this.

By colored plates he pictures the changes of blood smears due to this increased marrow activity, and in a specimen of blood taken from the marrow vein of a dog previously almost bled to death, he shows, besides the appearance of nucleated red cells, the presence of large lymphocytes.

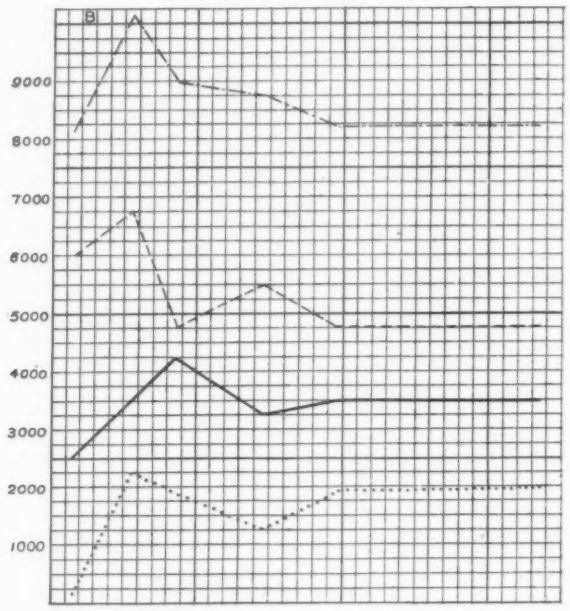
Following our observations on the effect of altitude in increasing the lymphocytes it was now argued that if bone-barrow hyperplasia provoked the increase of mononuclears reported, then artificial hyperemia of accessible bones might yield the same result. To this end a rubber bandage was applied as a tourniquet to the legs, as high up the thighs as possible, with sufficient pressure to interfere with the return venous flow, but not enough to obstruct the arterial.

The following chart represents the results of the first application of this method to man:



Mononuclear increase = 215%.
Polymorphonuclear increase=60%.

CHART TO SHOW EFFECT OF ALTITUDE (6000 FEET) ON HEALTHY MAN COMING FROM SEA LEVEL.



On arrival. 1 week. 2 weeks. 3 weeks. 3 months. 1 year.

Explanation of Chart —·—·—·—. Total leucocytes per cmm. - - - - - - Total polymorphonuclears per cmm. ———— Total mononuclears per cmm. ..... Large lymphocytes per cmm.

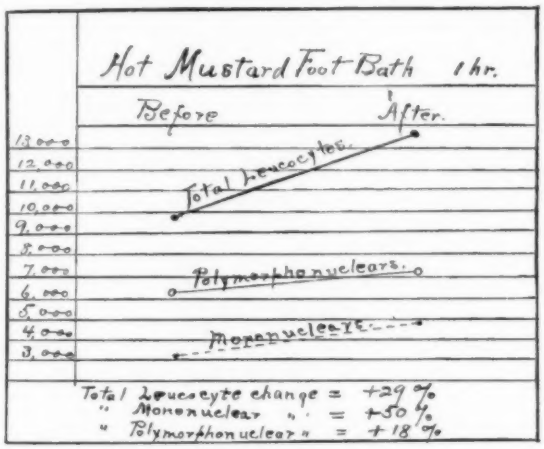
Notice overproduction of mononuclears after 2 weeks then drop. This would appear to be a similar biological phenomenon to Weigert's theory applied to the overproduction of amboceptors. Notice the same in regard to both red blood cells and lymphocytes in several of the Pike's Peak charts.

* The expedition discovered that at altitudes such as Colorado Springs and Pike's Peak, the lung cells themselves develop and secrete oxygen from the air and throw it into the blood. It was also conclusively shown that mountain sickness is due to lack of oxygen. The hæmoglobin and the red corpuscle counts were made by the members of the expedition, and are published by their courtesy.

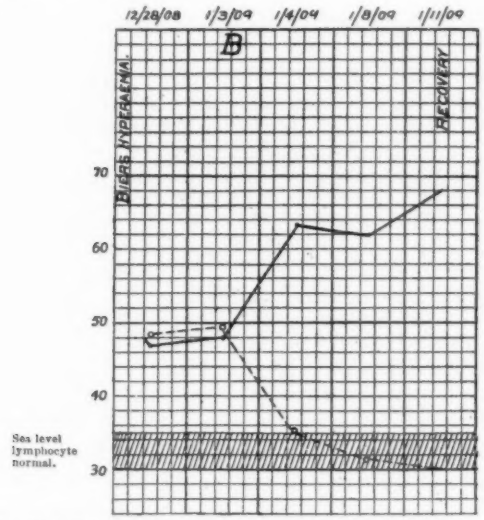
We found also that lymphocytosis could be produced by constant hyperemia of accessible long bones, as the following observations attest. The patients applied to their upper arms, day and night, a garter elastic, one inch wide, which was just tight enough to leave an indentation in the skin after removal. They suffered no discomfort, neither did the arms visibly swell. The following is an example:

Miss V. Turban III.—White blood corpuscles, 13,000. Lymphocytes, 29%. Two weeks hyperemia of both arms with garters: White blood corpuscles, 25,000. Lymphocytes 69%.

It was next questioned what the results of a hot mustard foot-bath might be on the blood picture; theoretically, it was expected a similar change would take place. The following is the result of such an experiment on a healthy male adult.



Several cases of tuberculous disease in the leg treated by Bier's hyperæmia yielded similar lymphocyte increase, as is seen in the chart below.



Small tuberculous abscess of tibia following blow received in hockey game.

—— Lymphocytes.
------ Polymorphonuclears.

We found with the continued arm hyperemia that about two weeks were required to produce the greatest results. After this time the patient's sputum will decrease, especially the thick yellow portion. In one patient who estimated that she expectorated her body weight in eight months the amount was reduced to one-quarter ounce daily. In some patients after several weeks treatment both temperature and pulse dropped.

The marrow as an organ is capable of enormous increase in work. The yellow marrow can be replaced by blood-forming marrow and even the bony lamellæ can be removed to make room for red marrow. We have used daily hot mustard foot-baths in order to provoke more activity in the bone marrow of the legs. Inasmuch as the fight against the tubercle bacillus is so largely one of blood cells the more marrow we can urge to work the better.

In some researches we conducted on rabbits we found that the red cells are also increased by marrow hyperemia, as the following tables show:

Normals—6 counts on 6 rabbits.....Average, 6,300,000
Normals—4 rabbits after one-half hour hyperemia .....Average, 8,100,000

Controls, R. 1, 2, 4, 5, and 6.....Average, 6,150,000
Hyperemias, R. 7, 8, 10, 11, and 12.....Average, 9,400,000

Being able to produce so large a lymphocytosis it was natural to question what would happen to the cell picture in the sputum. It was found that the lymphocytes appeared in the sputum in very large numbers, almost entirely replacing the polymorphonuclear cell.

Lymphocyte pus cells on careful searching could be found containing fragmented tubercle bacilli. With some patients the numbers of tubercle bacilli in the sputum appeared to diminish. That such cells appeared in the sputum indicated migration from the blood stream. The blood of such patients was therefore taken for opsonic tests. By means of these it was shown that the large lymphocyte and especially the large mononuclear and transitional cells had decided phagocytic powers. Making repeated observations at different intervals it was found that after forty-eight hours incubation some digestion and fragmentation of tubercle bacilli could be observed within these cells. The polymorphonuclear leucocytes did not seem to have this power.

The cover slip preparation of blood taken from individuals submitting to continued arm hyperæmia gave evidence of a large increase in blood platelets. We are at present attempting to ascertain the exact increase in these elements and also to determine whether they are increased by the effect of altitude, which we think possible.

The types of nongranular mononuclear cells increased by marrow hyperæmia are especially the large lymphocyte, the large mononuclear and transitionals. Occasionally also plasma cells are seen.

The effect of altitude and of bone marrow hyperæmia on the blood are therefore very similar to that of chronic carbon monoxide poisoning. In this, besides the increase of red cor-

pucles, an increase in the large lymphocyte element has been observed.

We have found this method of artificial lymphocytosis which brings with it some leucocytosis of value in other suppurations such as ear infections. It might prove of value in typhoid since the type of cells increased are similar to those increased in this disease.

It is possible that in the continued form of bone marrow hyperæmia other factors may influence the blood, such as oxidation products which may be retained longer than normally in the extremities.

Metchnikoff states that we are to accept it as a law that the leucocytes are capable of producing antibodies and that the microphages (polymorphonuclear leucocytes) must be regarded as the source of these protective substances in the blood and body fluids. However, he does not consider that they are secreted by the phagocytes. They are elaborated within these cells and are only capable of exerting any action after being set free, following the destruction of the cell—a process similar to that of the production of fibrin ferment due to the breaking down of leucocytes.

Using this conception of Metchnikoff's as a basis, Arneth[37] in 1904 published an exhaustive monograph on the behavior of the neutrophilic leucocytes in infectious diseases. He lays particular stress on the changes in the shape of the nuclei and divides the polymorphonuclear neutrophiles into five classes as follows:

Class I. Mononuclear neutrophiles.
Class II. Neutrophiles with 2 nuclei.
Class III. Neutrophiles with 3 nuclei.
Class IV. Neutrophiles with 4 nuclei.
Class V. Neutrophiles with 5 or more nuclei.

By averaging the counts on a number of normal individuals he finds the following percentages:

Class I.	Class II.	Class III.	Class IV.	Class V.
5%	35%	41%	17%	2%

While engaged in blood work we investigated the claims of Arneth with the results indicated in the following chart:

Class I.—Normal Adults.

55 Cases, 100 Counts.

	One Nucleus.	Two Nuclei.	Three Nuclei.	Four Nuclei.	Five and more Nuclei.
Average	8	36	42	13	1
Extremes	0–27	17–56	26–59	0.5–32	0–5
Mean	8	36	41	11	1

Arneth's Index: Average, 65; extremes, 50-86; mean, 67.

Class II.—Cured Cases of Pulmonary Tuberculosis.

58 Cases, 100 Counts.

Average	8	39	40	12	1
Extremes	0–35	20–60	23–59	2–32	0–6
Mean	8	40	40	11	1

Arneth's Index: Average, 67; extremes, 29-88; mean, 67.

Class III.—Improving Cases.

38 Cases, 100 Counts.

Average	10	41	39	9	1
Extremes 1.5–34		20–62	16–57	1–25	0–6
Mean	8.5	42	39	9	0.5

Arneth's Index: Average, 70.5; extremes, 47-91; mean, 71.

Class IV.—Stationary Cases.

37 Cases, 100 Counts.

Average	15	41	39	4	1
Extremes 0.5–49		10–62	10–52	0.5–32	0–7
Mean	12.5	43	35	6	0.5

Arneth's Index: Average, 75.5; extremes, 31-94; mean, 78.

Class V.—Advancing Cases.

25 Cases, 100 Counts.

Average	21.5	45	27	5.05	1
Extremes 2–50		10–62	10–51	0.5–37	0–11
Mean	20	49	28	4	0.3

Arneth's Index: Average, 80; extremes, 31-94; mean, 82.

Arneth considers the cells in the higher classes, those with the more complicated nuclei, to be the riper and more efficient—the ones capable of producing the most antibodies.

Bushnell and Treuholtz[38] conceived from this blood picture an arbitrary index made by adding together the percentages in Class I and Class II and one-half that in Class III.

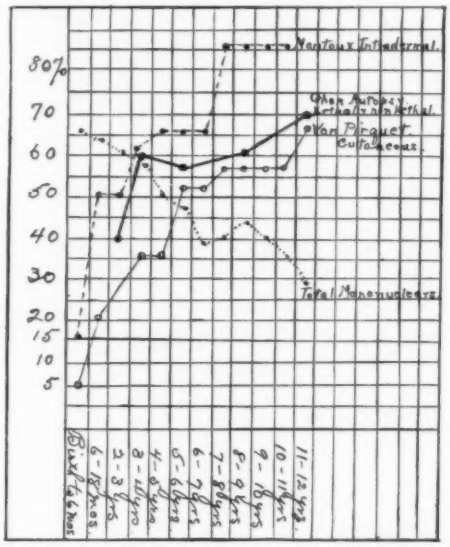
In studying the table we see that the averages of our counts in the various stages of pulmonary tuberculosis agree with the statements of Arneth; that, as a case progresses unfavorably, there is a decrease of the efficient cells, those in Classes III, IV and V, and an increase in the unripe cells, or those in Classes I and II.

Expressed in terms of Bushnell and Treuholtz's index, the higher the index, the lower the patient; but on closer scrutiny we note the great extremes in all the various stages. It is possible in the most advanced cases to get a blood picture whose index would be lower than the standard normal one, and among the normals to obtain one higher than the average for the most advanced cases. It is this extreme variability in the counts that has led us not to place too much value on isolated counts, though we do feel that a series of counts on a given patient gives us a certain idea as to the prognosis.

Diagnosis.

The following chart shows a great difference in the value of the cutaneous reaction and the intracutaneous reaction to tuberclin. It has been suggested that the intradermal test gives too many reactions, in other words, that non-tuberculous children and animals will react. But the chart also indicates that not so many children react to the von Pirquet test as autopsy records seem to require. It is extremely difficult when making repeated examinations to have children submit to the intradermal test. It is most important to make the most reliable test in children before and after submitting them to vaccination. It occurred to me, therefore,

to modify the "stick" reaction in the following manner, so that one can make an intradermal application of tuberculin with very little pain. We found that old tuberculin would dry on hypodermic needle points. These points are moistened with a drop of pure water placed on the sterilized skin and then plunged through the skin and given a twist as they are withdrawn. The reactions following this test are shown in the chart below. We have made about one hundred observa-



Note the drop in percentage of mononuclear cells or lymphocytes as age of child increases. As this occurs, the positive tuberculin reactions increase.

tions and we have found such tests positive when the von Pirquet test has been negative. The reaction is characterized by a definite lump, probably an actual tubercle. In two instances a slight temperature reaction followed this test. It is a test which children readily submit to repeatedly. The best location we find to be over the radial muscles, as here it is a very rare occurrence to puncture a vein, an incident which interferes with reaction.

It must be remembered too that children have a larger number of leucocytes than adults so that the change in absolute number of lymphocytes per cmm. from childhood to that of the adult would be a decrease from about 6000 per cmm. to about 3000 per cmm.

This occurrence may be of great importance in explaining the difference between tuberculosis in children and in adults.

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JOHN BELL, SURGEON. 1763-1820.

By EUGENE R. CORSON, M. D., Savannah, Ga.

"And gladly wolde he lerne, and gladly teche."

Read the writings of John Bell and you will see the greatness of the man and his nobility of character. Almost on every page you are aware of an intensity of conviction and a depth of feeling which come from a great mind and a great heart. I know no medical writer who is quite like him. His brilliant brother, Sir Charles, whose style charms you with its ingenuousness and warmth and color, is still very different. Generally speaking, the writers of a hundred years ago wrote in a way which seems to us stilted and formal beyond measure, and we weary of many pages. But John Bell has so much to tell us, and he is so anxious for his reader to know what he

has to teach, that his earnestness and his eagerness hold you, even when his argument is, perhaps, drawn out and he repeats himself. Sir Charles wrote as he was, simple, open-hearted, unaffected, with no rhetorical display, and yet with a nice use of words. You are aware that he writes to teach, but he is always more concerned with his own teachings than with the opinions of others, so that he is rarely polemical and never violent.

His brother John has also much to teach, but he is always concerned with the opinions of others; and when he sees their errors he will use every means to bring them out—the most incisive language, and even ridicule and sarcasm. Though usually dignified and most earnest, he may show humor, and even a broad humor which Sir Charles is inclined to apologize for. He is always the fighter, and the more prominent his antagonists the more ready he seems to attack. He never hesitates at high position, and is indifferent whether his antagonist is a contemporary or an old master in the profession. He brings out their errors, however, not simply to pick them out but to emphasize and teach what he regards as the truth. While free to censure he is equally free to praise, and he never omits an opportunity to show his admiration for the great Paré, or honest, bluff old Wiseman, or any old worthy, for that matter. Clearly as he has pictured for us the crudities of Frère Jacques, the savage jab of his dagger-knife, and his total ignorance of anatomy in the beginning of his work, he places him on a great pedestal in the Hall of Fame as the real originator of the modern operation of lithotomy, as one who cast to the winds the "apparatus major," and the perverted doctrine of Hippocrates that "wounds of membranous parts are mortal." But no matter what the subject, be it one in surgical pathology, or the application of a bandage, he writes with the same care and grace. And if his deeper nature be touched by the song of the nightingale, or by a scene in Florence by moonlight, he rises to the height of a fine impassioned prose.

John Bell came from good stock. His grandfather was a Mr. John Bell, minister of Gladsmuir, who was born on Feb. 2, 1676. He was noted for his industry, determination, and impressive eloquence, qualities all inherited by his grandson. He was called upon to preach the sermon on the death of William III before the General Assembly of the Church of Scotland. That he gained a reputation for a vigorous intellect before he was thirty shows him to have been a man of parts. He died at the early age of thirty-two, leaving several children, of whom William Bell alone comes into prominence as the father of four great sons, and as a member of the Catholic and Apostolic Church of Scotland. To have left the Presbyterian Church, of which his father and family were members, and to have become a minister of the Episcopal Church of Scotland, at a time when that church was under many restrictions and persecutions, shows his independence and fearlessness. His first wife, surviving all her children, died in 1750. In 1757 he married Margaret Morice, the elder daughter of an Episcopal clergyman. Early left an orphan, she was educated by her grandfather, Bishop White, afterwards Primus of Scotland. She was distinguished for her piety and many accomplishments, among which was a great talent for drawing which she transmitted to her children. She bore six children, of whom four sons rose to distinction, and even great distinction.[1]

Galton has found that the majority of men who reach eminence in science have had distinguished mothers, so that Charles and John Bell are no exceptions to the rule.

The eldest son, Robert, became an advocate and professor of conveyancing to the Society of Writers to the Signet, and was the author of the Scots Law Dictionary, and of several other works on the law of Scotland. He died in 1816. George Bell, the fourth son, was a distinguished jurist and professor of law in the University of Edinburgh. With the genius and distinction of Charles we are all familiar.

John was the second son, and was born on May 12, 1763, when his father was 59 years old. A month before his birth his father had been operated for stone, and his gratitude over his recovery led him to devote the talents of his son, born while he was convalescent, to the cause of medicine and to the benefit of mankind. Eleven years had to pass before the birth of his youngest son, Charles. Surely the operator in this case had much at stake, and his success deserved the perpetuation of his name, for at that time they had still much to learn of the operation, and the death rate was considerable.

John early showed his abilities. In the beginning he undoubtedly had the training of the home and the teaching of his distinguished mother, probably even more than Charles, who wrote so feelingly of his mother's influence and teaching. He was educated in the High School, and already showed a liking for medical studies. On entering the university he attended the lectures and practice of Black, Cullen, and Monro, Secundus, all famous names in the history of medicine. He was the special pupil of Mr. Alexander Wood, a prominent surgeon in Edinburgh. To him he dedicated the first volume of his Anatomy of the Human Body. While studying anatomy under the second Monro he conceived the idea of teaching the application of anatomy to surgery, a branch of instruction which Monro seems to have slighted. It became the dominant thought with him. He saw how the study of anatomy would dispel mere doctrines and hypotheses which did so much to retard the progress of medicine in all its branches. He saw the discipline which comes from the honest labor of dissection. As he writes in his preface:

> Of all the lessons which a young man entering upon our profession needs to learn, this is perhaps the first—that he should resist the fascinations of doctrines and hypotheses, till he has won the privilege of such studies by honest labor, and a faithful pursuit of real and useful knowledge. Of this knowledge, anatomy surely forms the greatest share. Anatomy, even when it is neglected, is universally acknowledged to be the very basis of all medical skill. It is by anatomy that the physician guesses at the seat, or causes, or consequences of any internal disease: without anatomy, the surgeon could not move one step in his great operations: and those theories could not even be conceived which so often usurp the

[1] See my paper on Sir Charles Bell. The Johns Hopkins Hospital Bulletin, 1910, XXI, 171.

place of that very science from which they should flow as probabilities and conjectures only, drawn from its store of facts.

In all his surgical writings this thought is ever uppermost. He taught it to his younger brother Charles, and when the latter published his Surgery he put on the title page "A System of Operative Surgery founded on the Basis of Anatomy." The value of this idea cannot be overestimated in the coming progress in surgery and the attainment of its present perfection. It was the first step. The second step came with anæsthesia, which permitted deliberate dissection of the living body; and the third step with Pasteur and Lister. I do not hesitate to place John and Charles Bell in line with these great names.

He must have graduated in 1785 or 1786, for in the latter year he became a Fellow of the Royal College of Surgeons of Edinburgh. Before beginning practice he traveled in Russia and the north of Europe. On his return he began at once to lecture on Anatomy and Surgery. In 1790 there was built for him a lecture theater in Surgeon's Square, where he gave regular courses of lectures and where he carried on his dissections and formed a museum. Until 1804, when his brother Charles went to London, he had his help as his demonstrator, as well as the use of his great artistic talent in the drawings of the dissections, and in the plates for publication. John Bell himself was no mean draughtsman, and he, too, etched or engraved many of his own drawings, as his works abundantly show. Charles, however, excelled him as an artist, though in artistic criticism John equalled, if he did not excell his brother. Charles' great System of Dissections, we must remember, was based on dissections made in his association with his brother. On several occasions Sir Charles refers to the critical and often severe tutelage of his brother. He speaks of him as his master, and in his annotated edition of the Surgery, published in 1826, he writes in the preface:

> It is with great satisfaction that I present to the profession an edition of Mr. John Bell's works; and did it not sound like vanity, I would express a wish that the contents of these volumes may prove to the reader of the same value that the lessons of a brother have been to me.

But John Bell was not of a nature to live a peaceful and uneventful life, however much absorption in scientific work tends towards peace and happiness. He was too much concerned with the opinions of others. His love of truth made him eager to detect error wherever he could find it, irrespective of time, place, or person, and proclaim it from the housetops, and in language of no uncertain meaning. He was not in the university and could speak out and write as he pleased, his own master and independent. In his lectures on the surgery of tumors, addressed to his late pupils, the first discourse is headed by a quotation from Chaucer: "Full gladly would he learn and gladly teach" (*sic*). This well-known line applies most aptly to himself. He was as great a teacher as he was a great surgeon. He did not agree with Cicero that from the false there was no truth to be learned, but rather from our mistakes we learned the most. So he would pick out the errors as he saw them, of friends or foes, to emphasize his teachings. He did not hesitate to criticize severely Dr. Monro as an anatomist and Benjamin Bell as a surgeon, which brought down a storm upon him. In 1799 appeared a pamphlet entitled "Review of the Writings of John Bell, Esq., by Jonathan Dawplucker,"[2] which attempted to exonerate Monro and Benjamin Bell from his unfavorable criticism, and also attempted to show that the first volume of his Anatomy was a plagiarism. John Bell replied by publishing a second number of the Review under the same name of Jonathan Dawplucker, addressed to Benjamin Bell, with severe reflections on his System of Surgery. He vigorously attacked the stereotyped methods of both Monro and Benjamin Bell. He had the students with him, and the book lost its popularity.[3]

But this was only the gathering of a storm which was to last several years, and which was to draw Bell into a most bitter and lengthy controversy, demanding much of his time and energy, and undoubtedly of injury to his health.

Dr. James Gregory, the Professor of Physic in the university, who besides his great intellectual brilliancy, had behind him his father's reputation, and the momentum of inherited power, conceived the idea of excluding the younger members of the Royal College of Surgeons from practice in the Royal Infirmary, on the ground that the patients suffered from the constant changes in treatment in the monthly rotation of the surgeons. Bell fought the measure at every step. He appeared before the Board of the Infirmary and produced six folio books, filled with surgical drawings and cases, as evidence of his system of teaching and his need of clinical material; but they turned a deaf ear to him. He then brought the question before the Law Courts, whether they had the power to exclude him, and it was decided against him. Though Gregory carried his point he was subsequently severely censured by the Royal College of Physicians for violations of truth and unprofessional conduct.

Bell was appointed by the Royal College of Surgeons of Edinburgh to reply to the Memorial of Gregory, which he did in an octavo volume entitled "An Answer for the Junior Members of the Royal College of Surgeons of Edinburgh to

[2] The writer of this anonymous attack was undoubtedly Professor Gregory, himself. In John Bell's Letters on Professional Character, etc., addressed to Gregory, p. 64, he writes: "With all your equivocations about Dawplucker, I well knew that under that title you threatened my character."

[3] Referring to Gregory's first anonymous attack on him, under the name of Jonathan Dawplucker, and his reply under the same name, he wrote in his Letters on Professional Character, etc.:

"In the first number was reviewed one volume of Mr. John Bell's System of Anatomy. In the SECOND was reviewed, in like fashion, the SIX VOLUMES of Mr. Benjamin Bell's System of Surgery. The advertisement was of the same form and of the same size; it was stuck up on the same board, and on the same gates and sticking places with the first. But this, Sir, was not like the advertisement of your friends, a mere brutum fulmen: I neither mistook my bird nor missed my shot: down came the offensive advertisement, which had been renewed and carefully kept in the public eye for many weeks, and down came the SIX VOLUMES, the whole covey at one shot, and never a leaf has fluttered since."

the Memorial of Dr. James Gregory, on the Edinburgh Infirmary." This was published in 1800.

But the controversy did not end here. Ten years later he published a work entitled "Letters on Professional Character and Manners, on the Education of a Surgeon, and the Duties and Qualifications of a Physician, addressed to James Gregory, M. D., Edinburgh, 1810, 8vo." Thus did his grievance rankle long in his breast, to the detriment of his health and happiness, and to the detriment of our profession, which could ill afford to give up any of his time and energy to such an ignoble cause.

Evidently the Royal Infirmary was not on the lookout for either genius or talent, for it promptly turned down Charles Bell's proposal to pay the Hospital £100 a year, and to transfer to it the museum he had collected, on condition that he be "allowed to stand by the bodies when dissected in the theatre of the Infirmary, and to make notes and drawings of ... diseased appearances."

This "Letters on Professional Character and Manners," etc. is indeed a most remarkable work, 636 pages of invective and righteous indignation, an expression of ten years of bitter controversy and professional strife. Gregory had seen fit in a quarto volume of 700 pages, full of scurrility and personal abuse, and even indecent jokes, to attack Bell and those junior surgeons whom he wished excluded from the Royal Infirmary. Copies of this work he had distributed gratis among friends and patients. He had even employed scurrilous handbills and posters distributed among the students and citizens generally. And to show him up to the world and to posterity Bell saw fit to write this book. Oh! the pity of it! that he should have been drawn into this strife! It was the great mistake of his life.

Brilliant as Gregory was and ever ready to quote his Virgil and Lucretius, he had an antagonist equally brilliant to answer him, and equally ready to quote from Latin literature and English literature, and to meet him on his own ground, and with his own weapons, and yet to be always the gentleman. Though Gregory gained his point, though he was the popular physician of the day and the brilliant lecturer in the university, and though fortune and prosperity followed him, I cannot accept Lord Cockburn's rather high estimate of his character. To me he seems mean and contemptible. He did no original work in science. He stands out a good example of mere intellectual brilliancy, as we use that term, without any abiding productiveness, or really contributing to anything.

It is a relief to pass from his polemical writings to his scientific works. The first volume of his Anatomy of the Human Body appeared in 1793, when he was thirty years old. In his preface he states very clearly his position in regard to anatomy and to his teachings to his students of this science, and in support of his position he quotes John Hunter, to whom he gives all praise as "the first anatomist and the truest physiologist of this or any age"; yet he does not hesitate to criticize him in his own peculiar way when differing from him. But not only in his Anatomy but in all his writings and teachings he tells his pupils to be an anatomist before being a physiologist, to study anatomy before taking up mere theories and hypotheses, and to be a good anatomist before attempting to operate upon the living body.

In 1794 appeared "Engravings explaining the Anatomy of the Bones, Muscles, and Joints, drawn and explained by the Author," quarto, Edinburgh. All the drawings and almost all the etchings and engravings are his own, sufficient evidence of his prodigious industry and labor. Volume II, on the Heart and Arteries, appeared in 1797, while Volume III, on the Brain and Nerves, the Organs of the Senses, and the Viscera, was the work almost wholly of Charles Bell. This Anatomy must stand in the history of medicine as one of the works which mark the progress of our science. If John Bell's drawings of dissections were sometimes rough, viewed from our standpoint to-day, they were honest drawings and no servile copies from other works, many of which had handed down from time immemorial the gross mistakes and fancies of copyists and imitators. Bell took pains to show many of these mistakes and their bearings on the grosser mistakes in surgery, especially as regards the surgery of the arteries. So far as I know he was one of the first who had a clear idea of the possibilities of the collateral circulation. The advances which were soon to follow in the surgery of the arteries, and especially in the surgical treatment of aneurism, of which he himself was a master, can truly be said to rest largely on his own anatomy of the blood-vessels. And I am not unmindful of the work of John Hunter, Sir Astley Cooper, and Abernethy in this branch. And when he came to apply this knowledge in his surgical discourses, it was to throw a flood of light upon the whole question. Looking back on these lectures after a quarter of a century, Sir Charles writes:

> **In considering this admirable discourse, every one with the slightest tincture of science, or capacity for it, must be struck with the evidence it affords, and satisfied of its great importance to every branch of surgical practice.**

The work was a popular one, went through several editions, and was translated into German when Germany was herself alive to anatomical study. In the preface to the first volume he states:

> **I have endeavoured to make it so plain and simple as to be easily understood; I have avoided the tedious interlarding of technical terms (which has been so long the pride of anatomists, and the disgrace of their science) so that it may read smoothly, compared with the studied harshness, and, I may say, obscurity of anatomical description.**

You see here the real love of the anatomist and the teacher.

In 1795 appeared his "Discourses on the Nature and Cure of Wounds." It seems strange to us to-day that it is not much over one hundred years ago that the profession was still largely influenced by the ancient notion that all wounds had "to mundify, incarn, and cicatrize," and that primary union was to be avoided as a dangerous shutting up of humors which had to be discharged. The opening sentence reads:

> **When a modern surgeon allows himself to talk about the "mundifying, incarning, and cicatrizing of wounds," or directs how to "fill the wound up with good and sound flesh, and keep it to a fair and even level with the adjacent skin," he but proclaims his own ignorance of the properties of the living body.**

Bell shows that the surgeon should strive to get primary union, that suppuration is a disease in itself, and that this primary union is obtained by smooth incisions, by as little disturbance of the tissues as possible, and a cut surface as free as possible from all oozing of blood, with the opposing surfaces carefully co-apted by adhesive strips and ligatures. He did not know what suppuration was, but he did know that too much disturbance and injuring of the tissues lead to suppuration. He was always careful not to close his incisions until all hæmorrhage had been controlled, and he writes of waiting fifteen minutes at times to assure himself that all oozing had ceased before he closed the wound. He writes:

> This adhesion, then, is a property of the parts of the living body, which is perfect only while their structure is entire; which operates only where the opposite parts touch each other by the fullest contact, and sympathize with each other in their period and degree of action. It is interrupted if any foreign body be interposed; it is less perfect in every unhealthy condition of the system; but it is a property of which we are now so well assured, that we look for its good effects in the greatest, as well as in the smallest, wounds; and the union of a hare-lip, after it has been cut and pinned, represents the perfection of that cure which we attempt in every greater operation, and more confidently in every smaller wound; succeeding sometimes as perfectly after an amputation of the thigh, as after the most trivial wound of the cheek.

How clearly he has expressed himself!

Bell's chief contribution to medicine was his anatomy and pathology of the arteries, and their application to the surgical treatment of aneurism; and in his Discourse II on wounded arteries we see how carefully he had studied the whole subject. We see here his skill in ferreting out from the literature the clinical cases to illustrate his teachings, and how clearly he sees their errors and what these errors teach. We can see how much old French and mediæval and inelegant Latin he must have waded through to pick out this material for his use. As he himself wrote he is looking for facts, without any regard to the writers' opinions; and the surer he is of his facts, the less he thinks of their opinions. Many of these old descriptions of cases are very interesting reading. There was a more studied and more elaborate description given to the surroundings and conditions of the case than we are apt to use to-day, which added to the picturesqueness and vividness, while we give, rather, a long inventory of the symptoms without any attempt at local color or a background. Of course our vastly wider horizon has multiplied the details, but I believe we could add much to the attractiveness and impressiveness of our clinical cases if we thought more of the literary form and the local color.

Through these cases we get glimpses of the practice two or three hundred years ago, the crudities and barbarisms which had come down through the centuries almost unchanged, up to the time of grand old Paré, whom Bell takes every occasion to praise and whose enemies he puts to shame. The crude notions of, and ineffectual efforts at checking hæmorrhage up to the time of Paré, and for many years after, in fact, are brought out to show more clearly the only proper way of controlling hæmorrhage, namely, by enlarging the original wound, by a careful dissection and separation of the artery, and the application of the ligature. It was later, however, when he published his Surgery, that he developed more fully his ideas of the surgery of the arteries and of aneurism. In this second discourse he shows us an interesting little bit of history relative to the femoral artery and its profunda branch, and how this latter had been overlooked by many, and even by the great Heister, and misunderstood by Mr. Gooch and Professor Murray. As a great object lesson he gives a striking drawing of a dissection of the femoral with its profunda branch as a frontispiece to the book.

Though more elaborately developed in his Surgery he shows how wonderful the possibilities of the collateral circulation are, and how fully equal to almost all cases where the main trunk is tied or diseased. And to show this he gives us a long detailed description of a case of stricture of the aorta, and one of the ascending vena cava. It is in this discourse that he gives us the history of his operation for an aneurism of the posterior iliac artery (the posterior branch of the internal iliac) in the case of the poor leech-catcher, and I make no apology for quoting the entire case, not only to show his surgical qualities but also his fine descriptive powers:

> A poor man, who was by trade a leech-catcher, fell as he was stepping out of a boat, and the long and pointed scissors which are used in his business being in his pocket, pierced his hip exactly over the place of the sciatic notch, where the great Iliac Artery comes out from the pelvis. The artery was struck with the point of the scissors, it bled furiously, the patient fainted; and in so narrow and deep a wound, the surgeon, when he came, found little difficulty in stopping it up, and less difficulty still in making it heal. The outward wound was cured; the great tumor soon formed; and the man traveled up from the North Country, where the accident had befallen him, and in six weeks after arriving in our hospital here with a prodigious tumor of the hip, his thigh rigidly contracted, the ham bended, the whole leg shrunk, cold and useless, as if it had been an aneurism on the fore part of the thigh.
>
> The tumor was of a prodigious size, and by that very circumstance of its being one of the greatest aneurisms, it lost all the characteristics of aneurism; especially there was no pulsation, no retrocession of the blood when the tumor was pressed upon; there was nothing peculiar except this, that the great and sudden distension was the cause of great pain; and from the continual pain, lameness, and his hopes of a cure, he was ready to submit to anything, beseeching us to operate.
>
> There was little doubt of its being a great aneurism, but there was a possibility of its being a vast abscess; and it was resolved, in consultation, that he should be carried into the operation room; that a small incision should be made; that the skin being cut, the bag itself should be just touched with the point of a lancet; and if found to contain matter should be fully opened; but if blood, that it was then to be considered as an aneurism of so particular a kind, as to entitle us to call for a full consultation.
>
> I made an incision two inches and a half in length; the great fascia in the hip, blue, and very strong, formed the coat of the tumor, and under that were seen the big fibres of the great Glutæus Muscle. The knife was struck into it, and large clots of very firm black blood rolled out by the tenseness of the tumor, which began to emit the clots in this way the moment that it was opened at one point. There was one thing further desirable before we put the patient to bed, that we should understand the case so far as to be able to report to the consultation, whether the artery

was absolutely open, and whether it was the great artery of the hip. I continued, therefore (knowing that the opening I had made could be covered with the point of the thumb), to pull out a few more clots of blood, till the warm and florid blood began to flow; I then pushed in a tent-like compress into the small wound of the tumor (viz. of the fascia), laid a broad compress over the outward wound, and put the patient to bed with one of the pupils holding the hand upon his hip.

This was done at one o'clock, and at four the consultation met, and the operation was performed. And in my notes I find two steps of the operation chiefly marked: First: That upon our opening the tumor fully with an incision of eight inches long, and turning out the great clots, the blood was thrown out with a whishing noise, and with such impetus that the assistants were covered with it, and in a moment twenty hands were about the tumor, and the bag was filled with sponges, and cloths of all kinds, which had no better effect than the cloths which, in any accident, the friends in great confusion wrap round a wounded arm; for though the blood was not thrown in a full stream, nor in jets, it was seen rising above the edges of the incision; it floated by the sides of the cloths which were pressed down by the hands of the assistants. But we knew by a more alarming sign that the artery was throwing out blood; for the man, who was at first lying, not flat, but supporting himself on his elbows, fell down, his arms fell lifeless and without pulse over the side of the table, his head hung down and was livid, he uttered two or three heavy groans, and we believed him dead.

Secondly: Seeing in this critical moment that, if he was to be saved, it could be only by a sudden stroke, I ran the bistoury upwards and downwards, and at once made my incision two feet in length: I thrust my hand down to the bottom of the tumor, turned out the great sponge which was over the artery, felt the warm jet of blood, and placed the point of my finger upon the mouth of the artery; then I felt distinctly its pulse, and then only was I assured that the man was still alive. The assistants laid aside the edges of this prodigious bag, and sought out the several sponges which had been thrust in, and the bag being deliberately cleaned, and its edges held aside, I kept the forefinger of my left hand steady upon the artery, passed one of the largest needles round under my forefinger, so as to surround the artery: one of my friends tied the ligature, and then upon lifting the point of my finger, it was distinctly seen, that it was the Posterior Iliac Artery,—that the artery had been cut fairly across, and had bled with open mouth—that it was cut and tied exactly where it turns over the bone: and although the extremities were cold, the face of a leaden colour, and the man had ceased to groan, and lay as dead; though the faint pulsation could not be felt through the skin in any part of the body; we saw the artery beating so strongly, whenever I lifted my finger, that we were assured of our patient's safety; however, he was so low that, after laying down the sides of the sac, and putting bandages around the body to keep all firm, we were obliged to have a bed brought in, and having given him some cordials, we left him to sleep in the great operation room, attended by the pupils and by nurses.

This patient recovered though it took seven months to complete the cure. It is indeed worthy of republication and I trust another admirer of John Bell a hundred years hence will republish it. A great poem is an inspiration, and a great effort to save a human life is an inspiration; they both have the same source.

In all wounds of the arteries he urges the importance of enlarging the original wound, especially in punctured wounds, and picks out from the literature interesting cases showing the mistakes made by approaching the vessel by a new incision, though the usual route, and missing the punctured wound in the vessel. These clinical cases are analyzed with great skill and minuteness. It was a form of wound more common then when the practice of duelling was universal.

His discourse on gun-shot wounds was based on much practical experience. It will be remembered that his brother Charles went down to Portsmouth to study gun-shot wounds after the battle of Corunna, and later to Brussels after the battle of Waterloo for the same purpose. In 1798 John Bell visited Yarmouth to study gun-shot wounds among the seamen of Lord Duncan's fleet wounded at Camperdown. This led to his writing "A Memorial concerning the Present State of Military Surgery." He showed further his zeal in 1803 when Great Britain seemed threatened by an invasion of Napoleon, by offering his services to the government to form a corps of young men instructed in military surgery and the duties of the camp and hospital, with the view of their being helpful in the defense of the country. Like Sir Charles he was busy with his pencil and brush, and some of his drawings of the wounded adorn his System of Surgery. His proposal was first accepted but later declined as unnecessary.

Along the same lines he treats of wounds of the sword and bayonet, or any clean-cutting weapon, and then passes on to wounds of particular parts, the head, the breast, and the abdomen. He properly preferred enlarging the wound with the knife rather than with setons and tents, and could avoid making fun of Mr. Benjamin Bell for his use of these instruments.

He treats at length of wounds of the chest and lung, he saw the value of free incision and drainage in empyema, and understood thoroughly the value of a collapsed and non-functioning lung where there is an opening in the chest or there is fluid or air in the pleural cavity. His views of wounds of the peritoneum are interesting in the light of present-day advancement. He knew, of course, and quotes cases as examples, that many an apparently fatal wound of the abdomen is recovered from. He was fully aware that the abdominal cavity, so-called, was not a cavity. He writes:

Soldiers recover daily from the most desperate wounds; and the most likely reasons that we can assign for it are: The fullness of the abdomen, the universal, equable, and gentle pressure, and the active disposition of the peritoneum, ready to inflame with the slightest touch; the wounded intestine is, by the universal pressure, kept close to the external wound, and the peritoneum and the intestine are equally inclined to adhere; in a few hours that adhesion is begun which is to save the patient's life, and the lips of the wounded intestine are glued to the lips of the external wound.

It was on this reasoning that he advised but a single stitch for the intestine cut across:

The two ends of the gut may be made to adhere to each other; and the prudent way of favouring these adhesions is to introduce the one piece of intestine a little way within the other, and to make one single small stitch in that part of the circle which is farthest from the mesentery, and then draw the gut by means of that thread close up to the wound, and thus it will probably happen, that the mesentery will keep its side of the circle firm, that the stitch will keep the opposite side firm, that the gut being drawn by the thread, and pushed from behind and flattened by the universal pressure within the abdomen, the double adhesion may take place.

Benjamin Bell in his Surgery had advocated the complete stitching around of the intestine and so figured it in his work, and John Bell reproduces the figure alongside his own to contrast the two. He gives no cases to show he had ever employed this method. Benjamin Bell's plan, while it may in one way seem more surgical to us to-day, even with the conditions then existing, is quite impossible from another standpoint and is evidently a mere fancy. John Bell's, though it seems to show a timidity, must be ascribed rather to a constant tendency with him to simplify operations. He never feared large incisions, but he is ever warning his pupils against "piddling" work, as he inelegantly characterizes it. Later in his life, when the profession deprecated the radical operation of ovariotomy, he upheld it as a proper procedure, though there is no record of his having done the operation. After Ephraim McDowell, who was one of his pupils, had operated successfully, he sent his MS. to his preceptor for his perusal and approval, but he had already left for Italy, and the MS. was read by John Lizars, who was doing his work. This may explain how the latter was the first to follow in Houstoun's footsteps, for he did the operation successfully on Feb. 27, 1825, using the long ligature, which, by the way, was the ligature for the ovarian stump that John Bell's was for the intestine.

The idea prevailed for centuries that atmospheric air was noxious when introduced into the closed cavities of the body. It was prevalent one hundred years ago; and even after the introduction of antiseptics it was hard to dispel this notion, and the earlier antiseptic operations were done under the spray. Bell takes pains at some length to dispel this idea, and he does it in the strong language of his firm convictions.

His discourse on wounds of the head is admirable even in the light of to-day. It was to be further elaborated in his System of Surgery, where he introduced many interesting cases from the old masters to show the errors of the day and to teach the principles he thought correct. He draws for us fine clinical pictures differentiating concussion and compression and the indications for the trepan. He shows how this operation was abused, how they trepanned for everything, and with dreadful mortality; and not only once but many times in a wild effort to find something. He quotes the advice of Heister:

> In these cases it will be necessary to trepan first on the RIGHT side of the head, then on the LEFT side; afterwards upon the FOREHEAD, and lastly upon the OCCIPUT, and so *all round* until you meet with the seat of the disorder.

The last part of this work deals with dangerous wounds of the limbs and the question of amputation. He advises his students to read Le Dran, who says: "Wherever there plainly is a necessity for losing a limb, the sooner it is done the better"; and then to read Mr. Belguer, who exclaims: "To cut off a limb after a bad wound, what is it but to add wound to wound?" With rare judgment he points out the two sides of the question, enjoins his students to study each individual case freed from mere opinions.

> When your opinion is called for, pronounce it boldly; and say, if you think it right to say so, "This limb must be cut off." But when you are prevented by officious relatives, or if the patient should refuse his consent, when the accidents of the case interrupt you, or you are in a confused or dangerous camp, where operations cannot be done, then do what remains of your duty—not with the ill humor of a man thwarted in some little view, or smarting under the sense of a disappointment or affront—set yourself heartily and kindly to save your patient's limb and his life.

And he begins his last discourse: "The best operations are sometimes abused, and so is amputation abused: the most dangerous remedies are sometimes required, so is amputation." The whole chapter is clear thinking and good writing.

The first volume of the Principles of Surgery appeared in 1801, in quarto, with the title: "The Principles of Surgery, of the ordinary duties of the Surgeon; containing the Principles of Surgery as they relate to Wounds, Ulcers, and Fistulas; Aneurisms and Wounded Arteries; Fractures of the Limbs; and the Duties of the Military and Hospital Surgeon; with plates accurately colored from Nature."

The second volume appeared in 1806, "Containing the Operations of Surgery; viz., the Anatomy and Pathology of the Skull and Brain; in the form of Discourses on the Structure and Diseases of the Skull; the Structure and Diseases of the Brain; on Apoplexy, Palsy, Hydrocephalus, Phrenzy, the various species of Fractures of Skull and the Operation of Trepan."

The third volume appeared in 1807, being "Consultations and Operations on the more important Surgical Diseases, containing a Series of Cases calculated to illustrate chiefly the Doctrine of Tumors, and other irregular parts of Surgery: and to instruct the young surgeon how to form his prognosis and plan his operations. 37 Plates."

The work was popular and had a good sale in spite of its being expensive.[4]

In 1826 a new edition appeared under the supervision of Charles Bell in 4 Vols. 8vo. In the preface he writes:

> It has been my object in republishing these volumes, to retain all the important practical matter—to preserve, also, the admirable introductions, as well as the lively and ingenious illustrations. But in the original edition, the work was loaded with notes, containing long Latin quotations, and unnecessarily encumbered with excerpts from obsolete French works, ... I had long observed with regret that the admirable lessons contained in these works were to be got at with too much expense and labor, and that they were thus lost to the practising part of the profession.

The work to us is chiefly of value for its historical treatment of the principles it sets forth. Not only has there been a skillful use of clinical cases to illustrate these principles, but he has given us glimpses of the practices in the past. In his history of the doctrine of adhesion, for example, we have an interesting account of the professional suckers. No duel was complete without the presence of one such, who promptly

[4] In the publisher's advertisement we read: "The Principles of Surgery. By John Bell. In 3 volumes. Royal 4to. Illustrated with numerous engravings, many of them accurately colored from nature. Price £11, 11s. in boards, or each volume may be had separate. Vol. 1, price £4 4s. Vol. 2, £5 5s. Vol. 3, £2 2s."

sucked the punctured or incised wound, and applied a wad of chewed paper. The trade was not without its emoluments, for Verduc observed, "Suxerunt quidem, at non sanguinem sed potius aurum."

In the chapter on Hospital Gangrene, and, in fact, on many other occasions, we are shown the conditions existing in the great Hôtel Dieu at Paris. Bell called it "that great storehouse of corruption and disease," where this gangrene raged without intermission for two hundred years. "A young surgeon (says an ancient French author) who is bred in the Hôtel Dieu, may learn the various forms of incisions, operations, too, and the manner of dressing wounds; but the way of curing wounds he cannot learn. Every patient he takes in hand (do what he will) must die of gangrene."

The history of the treatment of hæmorrhage down to Paré, and the different methods of applying the ligature since his time, are well described. He thus leads up to his own views of the pathology and of the surgical treatment of wounded arteries and aneurisms, which form, I think, his greatest contribution to surgery. He taught the same great lessons in the surgery of the arteries which are taught to-day; that it must be a surgery founded on anatomy, that the collateral circulation is fully equal to the tying of any large arterial trunk; that the artery should be tied with the least disturbance of the surrounding tissues. While he fully appreciated the value of the Hunter operation, the technique of which he certainly improved upon, he saw that in the surgical treatment of aneurism there was a better method still, namely, to apply the tourniquet, lay open the aneurismal sac its entire length, dissect out the proximal end of the artery and tie it properly, avoiding other arteries and nerves in the ligature—then tie the distal opening—and "instead of merely cleaning away the great clots of blood, so as to see the wounded artery, we should wash and sponge it with particular care, fill it slightly with caddis or scraped lint, and compress it moderately with a general bandage." Even Sir Charles in his commentary twenty-five years later did not see that this was really an advance on the Hunter operation, for he wrote:

> But my master is here describing a circumscribed aneurism. .... You do not cut up a natural aneurism but tie the artery above it; so you may do here in a punctured artery, if the tumor be small and circumscribed.

John Bell really did and preached the Matas operation, lacking, of course, the asepsis, and the sewing up of the sac and wound as a natural sequence of the asepsis.

One point in the technique which he impressed upon his students with great emphasis, was not to trust to digital compression of the artery above the seat of operation—as stopping the pulse did not stop a dangerous flow of blood from the exposed or cut vessel—but to use the tourniquet.

In doing the Hunter operation he applied two ligatures and cut between, to allow each cut end to retract among the muscles, his idea being to imitate the tied artery in the stump of an amputation. He knew that there was less chance of secondary hæmorrhage from the stump of an amputation than from an artery tied in its continuity, and he explained it by the tied artery retracting among the muscles, which, by immediate cohesion or subsequent inflammatory exudate, helped to close permanently the vessel. He had tied most of the great vessels, the common carotid successfully, but failed on the external iliac, the man dying half an hour later from collateral hæmorrhage.

He devoted much space to the treatment of fractures, the nature of callus, and the vitality of bone itself, and you can see that bone was to him just as vital a tissue as the softer tissues. He pays most attention to fractures of the neck of the femur and of the patella, and differentiates in a very striking way between intra- and extra-capsular breaks, urging his pupils to base their pathology and treatment on the study of museum specimens. When Sir Charles published his beautifully illustrated work entitled "Observations on Injuries of the Spine and of the Thigh Bone," he wrote:

> Every question connected with the surgery of the thigh bone can be illustrated without going out of my museum, where there are thirty-seven examples of fracture of the body of the femur, independent of those of the neck; all these have been collected under the impulse given by my brother's impressive lessons on the importance of facts. I hope what I have delivered will convey to my hearers the same sentiments, and have with them a similar effect, teaching them to mistrust everything but anatomical proof.

Practically an entire volume is devoted to tumors, their nature and surgical treatment, with careful clinical descriptions of some of his own cases. He taught in no uncertain terms the importance of the removal of all tumors in the beginning of their growth. He gives a long discourse on the unlimited growth of tumors; on tumors of the bones; on tumors of the nostrils, gums, and throat, and especially on polypus. Some of his own cases of malignant growths of the parotid gland, lips, and cheek, operated on in a radical way, show fine dissection and surgical skill.

I know no separate work on the history of lithotomy and the development of the perineal operation as now done. Bell has written for us this history, covering two hundred and forty-eight pages, 8vo., and a clearer and more interesting chapter in the history of human endeavor I have never read. I could recommend any publisher to publish this history just as it stands. He has shown us how a great discovery may come to us from an humble source; that a great truth may find a ready acceptance with the unlearned, and meet its fiercest opposition with the "learned," as we use that term, and with those in high places. As he traces the modern operation back to Frère Jacques thus does he characterize him:

> Thus do we owe to this illiterate man, whose modesty, humility, and courage, whose charity, simplicity, and goodness, we must hold in respect, an operation which has been approved of, and performed by all the good lithotomists of Europe; and from his life and fortunes, one important lesson may be deduced; we may learn how slightly we should rely on our natural talents, how little faith we should have in mere courage!—this intrepid, fearless man committed nothing but butcheries, while he remained what has been termed a natural operator; but after having undergone the discipline of science, and learned the anatomy of the parts, he became truly valuable.

I have indicated Bell's controversial powers, and the constant tendency with him to fight for the truth as he saw it. I have tried to show as briefly as possible his great qualities as an anatomist, as a surgeon, and as a man of science. And now I would show another side of the man, in its way just as great, and more wonderful, perhaps, as so rarely seen coupled with high scientific attainments. I refer to his artistic talents and his love of the beautiful in nature and art. His brother Charles possessed this quality also, and while more skillful with the pencil, was, perhaps, less gifted as an art critic and interpreter of the beautiful; or, perhaps I should rather say, in his ability to give expression to the thought and the feeling when they mingle.

Early in 1816 he was thrown from his horse, which was the beginning of ill health which never left him. In 1817, with the hope of recovering his health and strength he started with his wife for Italy. Even at the beginning of his journey, before leaving Paris, he was evidently aware of the serious nature of his illness, for he had jotted down in his note-book, so full of fine observations on art and architecture:

I have seen much of the disappointments of life. I shall not feel them long. Sickness in an awful and sudden form; loss of blood, in which I lay sinking for many hours, with the feeling of death long protracted, when I felt how painful it was not to come quite to life, yet not to die, a clamorous dream! tell that in no long time that must happen, which was lately so near.

And yet with this consciousness of the approaching end, he wrote out, with the same interest and industry he had written out his voluminous clinical records, his impressions of travel, and of the art and architecture of Italy which he had learned to love with all the ardor of the southern nature. In his youth he had enjoyed the wild scenery of his own land, and had shown a quick and delicate responsiveness to the beauties of nature. And now in this Italy of blue sky and sea, of the olive and the orange and the grape, with the glories of Greece and Rome still lingering, and with its own glories on every hand, he could forget his declining strength, and revel in the beauties about him. As we read these criticisms of the great masters, of the churches which the spirit of Christianity as well as the spirit of architecture itself had both wrought, we find a nature as sensitive, as clear to see the wonders of genius and the beauty of the flower by the roadside, as any real poet or true lover of the Earthly Paradise. If you will read his "Observations on Italy" you will see this lover of the Earthly Paradise, and his power to give expression to his love.

I cannot forbear quoting for you a page or two. He is wandering late in the night through a silent part of Florence, enjoying the solitude about him, and the great buildings in the moonlight, and thrilled by the occasional song of the nightingale, when he comes suddenly upon a procession of the Brethren of the Misericordia:

Traversing the great centre of the city, along streets darkened from the height of the buildings, I passed along these immense edifices with strange feelings of solitude, as if in a dream, as if the gay and peopled world had vanished, and these gloomy mementos of the past alone remained. It was night, and in this distant spot not a soul was stirring, not a foot was heard, when, on crossing a narrow alley, the prospect suddenly opened, and the slanting rays of the full moon, falling with a softened light among the magnificent monuments of ancient times, displayed a splendid scene.

At that moment the tower bell of the prison struck loud and long, tolling with a slow and swinging motion, seeming, from the effect of reverberation, to cover and fill the whole city; even in day this bell is distinguished from any I ever heard; but in the dead silence of the night it sounded full and solemn. Impressed by the feeling excited by the grandeur of the scene, I still prolonged my walk, and insensibly wandered on. The silence of night was unbroken, save by an occasional distant sound, arising from the busiest quarter of the city, or from time to time by the song of the nightingale, which reached me from the rich and beautiful gardens that skirt the walls of Florence, recalling to my mind the voice of that sweet bird, as I heard it when detained in the narrow valley of the gloomy Arco. I remember how its little song thrilled through the long melancholy of the night, a lengthened, oft-repeated note, which still came floating on the air like a light sleep. Involved in these musings of lulled and idle thought, I suddenly beheld in the distance, issuing from the portals of a large edifice, forms invested in black, bearing torches, which, casting a deepened shadow around, rendered their dark forms only dimly visible. Still increasing in numbers, as they emerged from the building, they advanced with almost inaudible steps, gliding along with slow and equal pace, like beings of another world, and recalling to mind all that we had heard or read of Italy, in the dark ages of mystery and superstition. As they approached, low and lengthened tones fell upon the ear; when the mournful chanting of the service of the dead told their melancholy and sacred office. The flame of the torches, scarcely fanned by the still air, flung a steady light on the bier which they bore, gleaming with partial glare on the glittering ornaments, that, according to the manner of this country, covered the pall.

I looked with a long fixed gaze on the solemn scene, till, passing on in the distance, it disappeared, leaving a stream of light, which, lost by degrees in the darkness of night, seemed like a vision. The images presented to the mind had in them a grand and impressive simplicity, a mild and melancholy repose, which assimilated well with the hopes of a better world. It seemed like a dream, yet was the impression indelible.

Of the ordinary incidents of his life, and of those human qualities which had to do with his every-day life, I can gather but scant mention. In 1805 he married Rosina, daughter of a retired physician, Dr. Congleton. The marriage seems to have been a happy one, though childless like his brother Charles's. Mrs. Bell, five years after his death, published his notes on Italy, entitled "Observations on Italy." It was edited by his friend Bishop Sandford, of Edinburgh. A second edition appeared in 1835, with his additional notes on Naples. Mrs. Bell gives us a glimpse of his character in the preface. She writes:

With warm affections and sanguine temper, he still looked forward with the hope that his labours and reputation would one day assuredly bring independence; and meanwhile, listening only to the dictates of an enthusiastic nature, and yielding to the impulse of feeling, he would readily give his last guinea, his time and his care, to any who required them. Judging of others by himself he was too confiding in friendship, and too careless in matters of business; consequently from the one he was exposed to disappointments, and from the other involved in difficulties and embarrassments which tinged the color of his whole life.

Although his income was large he seems to have lived in a style beyond his means. He lived at No. 9 George Street, at

that time a fashionable part of the new town of Edinburgh. He probably entertained much, for his musical parties were celebrated. His social gifts were many, especially his great conversational powers, with great learning, classical and artistic, and much general information. Sir Charles, in one of his letters to his brother George, referring to the life of his brother John, which he had written but decided, unfortunately, I think, not to publish, wrote:

He did dunch and press one; but since I lived with him I have scarcely enjoyed what may be called conversation.

I have failed to find any portrait or sketch of him. He is described as "below the middle height, of good figure, active looking, and dressed with excellent taste, keen and penetrating eyes gave effectiveness to his regular features, so that his expression was of a most highly intellectual type."[5]

There is a strange fascination which distance lends, be it of time or space, and we long to look closely at the great figures of the past to see exactly how they appeared. We long to touch something which they had touched, so that an autograph letter, or any little bit of personal belongings becomes quite priceless. So far I have failed to get anything to gratify this desire.

He died in Rome on April 15, 1820, dropsical and in great pain and suffering, and was buried in the Protestant cemetery. Sir Charles, in a letter dated June 4, 1840, wrote:

Went to poor John's grave. The Pyramid of Cestius attracts you from a distance. A plain stone marks the place as you enter the ancient reformed burying ground. A single antique column is between the enclosure and the pyramid. Remembering old times, a fitting resting place.[6]

Thus lived and died a great surgeon and a great man. He stood between the old medicine and the new; he saw the errors of the old, and helped prepare the way for the new. He was a worthy follower of John Hunter, for he taught a surgery on the basis of anatomy, and a pathological anatomy above all mere theories and opinions of disease; and last but not least, he taught a deliverance from mere authority and tradition by honest and ever vigilant investigation.

Nullius addictus jurare in verba magistri,
Quo me cunque rapit tempestas, deferor hospes.

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5. Answer for the Junior Members of the Royal College of Surgeons of Edinburgh, to the Memorial of Dr. James Gregory, on the Edinburgh Infirmary. Edinburgh, 1800. 8vo.

6. Memorial concerning the Present State of Military Surgery. Edinburgh, 1800. 8vo.

7. The Principles of Surgery: Vol. I. Of the Ordinary Duties of the Surgeon; Containing the Principles of Surgery as they relate to Wounds, Ulcers, and Fistulas; Aneurisms, and Wounded Arteries; Fractures of the Limbs; and the Duties of the Military and Hospital Surgeon. With Plates accurately colored from Nature. Edinburgh, 1801. 4to. Vol. II. Containing the Operations of Surgery, viz.: The Anatomy and Pathology of the Skull and Brain; in the form of Discourses on the Structure and Diseases of the Skull; the Structure and Diseases of the Brain; on Apoplexy, Palsy, Hydrocephalus, Phrenzy, the various Species of Fractures of the Skull and the Operation of Trepan. Edinburgh, 1806. 4to. Vol. III. Being Consultations and Operations on the more important Surgical Diseases. Containing a Series of Cases calculated to illustrate chiefly the Doctrine of Tumors, and other irregular parts of Surgery: and to instruct the young surgeon how to form his Prognosis and plan his Operations. 37 Plates. Edinburgh, 1807. 4to.

8. Letters on Professional Character and Manners, on the Education of a Surgeon, and the Duties and Qualifications of a Physician, addressed to James Gregory, M. D. Edinburgh, 1810. 8vo.

9. Observations on Italy: Posthumous work, edited by Bishop Sandford of Edinburgh. 1825. Second Edition, 1835 (including John Bell's Notes on Naples).

10. Dictionary of National Biography. Edited by Leslie Steven and Sydney Lee. The Macmillan Co. London and New York, 1908. Article John Bell.

11. The Scottish Nation; or the Surnames, Families, Literature, Honours, and Biographical History of the People of Scotland. By William Anderson. Edinburgh and London, 1880. Article John Bell.

12. Biographical Dictionary of Eminent Scotsmen. By Robert Chambers. Glasgow, 1834. 4to.

13. Edinburgh under Sir Walter Scott. By W. T. Fyfe. With an Introduction by R. S. Rait. New York. E. P. Dutton & Co. 1907.

[5] Chambers' Eminent Scotsmen.

[6] In 1869 Sir James Y. Simpson visited the grave and had the stone repaired as a mark of his admiration.

JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice; abstracts of papers read and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly. Volume XXIII is now in progress. The subscription price is $2.00 per year.

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SOME SUGGESTIONS TO THOSE UPON WHOSE AID THE SUCCESS OF THE OPHTHALMIC SURGEON, IN CONSIDERABLE MEASURE, DEPENDS.*

By Samuel Theobald, M. D.,

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However skilful the ophthalmic surgeon may be, the results of his work are materially influenced by the efficiency or lack of efficiency of those upon whose aid he must, in no inconsiderable measure, depend. An awkward surgical assistant, a nurse ill-trained or without aptitude may, with the best intention, perhaps, bring to naught his most painstaking efforts, and convert an operative procedure which otherwise would have been a success into a partial or complete failure. Every oculist who has operated extensively doubtless can recall such an experience. It has seemed to me, then, well worth while to offer some practical suggestions to those whose duty it is to supplement the work of the ophthalmologist.

The Surgical Assistant.—As of greatest importance, may be considered, first, the services of the surgical assistant. In many minor operations lack of skill or experience upon his part may be an inconvenience only; in other more important and delicate ones the success or failure of the operation may hinge upon it.

The assistant's first duty, it may be said, is to learn, for example, in "fixing" the eye, to keep his hands out of the operator's way. This is always practicable, and with a little study the art can easily be acquired. A steady hand, on his part, is also essential, and, if he will observe his chief, he will find that this is attained by resting the wrist or some part of the hand—the ring, or little, finger most probably—upon the patient's cheek or forehead. Few, if any, ophthalmic surgeons operate "from the shoulder." Again, if his fixation is to be satisfactory, he must grasp the conjunctiva—and a fairly broad grasp it should be—close to the corneal limbus, otherwise the loose conjunctiva will stretch, and the eye will not be held securely. If he is asked to rotate the eye in a certain direction, he must not simply *pull* it in this direction, but, bearing in mind the ball and socket-like movements of the eye resulting from the conjoint action of the straight and oblique muscles, he must really *rotate* it in the direction indicated. And in all such maneuvers, of course, he should be careful to exert a minimum amount of pressure upon the eyeball.

The sponging of an eye during a delicate operation, such as cataract extraction, deserves almost to be ranked as an art. For myself, I do not like dry sponging, but prefer the sponge should be dipped in a sterile boric solution, and then squeezed nearly dry before it is used. I also make it a rule, and I regard it as of real importance, that in such operations the assistant shall not sponge the eye unless he is directed to do so, and he is further cautioned to avoid, as far as may be practicable, bringing the sponge in contact with the cornea.

There is a certain maneuver, hard to describe, and, it would seem, not easily learned by the average assistant—perhaps, one might describe it as a momentary pressure followed by a gentle wipe—that is most effectual in removing coagulated blood from the conjunctival sac. It is often very helpful to the operator, and he is fortunate in having an assistant who has acquired the knack.

The elevation of the upper lid, in addition to that afforded by the speculum, in some cases facilitates the work of the surgeon. The assistant should do this with the forefinger, being careful to avoid pressing upon the eyeball. Another most helpful service he will occasionally be called upon to perform, is to exert counter-pressure upon the scleral margin of the section, to facilitate the extrusion of an obdurate cataract—one, perhaps, with an exceptionally large nucleus. In doing this he should gently depress the upper edge of the wound with a Daviel's curette, so as to cause the section to gape slightly, being careful that the instrument does not obstruct the exit of the lens; and when the lens is well engaged in the section, if called upon to do so, he may help to deliver it with the curette, by lifting or rotating its margin through the wound.

The assistant who can do all the things I have enumerated, just as the operator would have them done, if, perhaps, not worth quite his weight in gold, as the phrase runs, is, at all events, worth more than a score of helpers who can do them only in tolerable fashion.

The Nurse.—One of the most helpful advances in modern medicine and surgery, as all will agree, has been the providing of the trained nurse; but, until she has had very special training, she is not as helpful to the ophthalmologist as could be wished. For example, she has little appreciation of the delicacy of his instruments; she cannot understand, as I have learned to my sorrow, why a cataract or an iridectomy knife should not be put, loose, in the tray of an instrument case intended for forceps, needle-holders and artery clamps, or why his cutting instruments should not be boiled as long as his speculum or strabismus hook, or why they should not be boiled after, as well as before, an operation. A sponge is a sponge to her, and she fails to comprehend why the eye-surgeon makes such a pother about its size. In using an eye-dropper, she commonly holds it upside down, and she is as apt to place the candle, for oblique illumination, behind the patient's head as she is to hold it in front of it for an ophthalmoscopic examination.

She speaks of a fifty per cent solution of boracic acid, when she means a saturated solution which has been reduced to half this strength—about two per cent—by the addition of water; and, if the operator is so indiscreet as to permit her to wash and dry his cutting instruments, he, not improbably, will later

* A paper read before the American Ophthalmological Society, June 12, 1912.

realize his indiscretion. She offers to flood the room with sunlight for a first inspection after a cataract extraction, and wonders why he should prefer the dim light of a single candle, which she finally procures for him, after much diligent searching.

However, if she is reasonably intelligent and observing, and has had the advantage of a well-conducted training school, it will not require many weeks in an ophthalmic hospital to eliminate these particular shortcomings, and, assuming she is interested in the work, she will presently be as dependable and as helpful to the surgeon in her new field of labor as she was in the routine of the general hospital.

She will soon learn that the keen edge of a cataract knife will not stand more than thirty seconds' boiling, and that the slightest rough usage will blunt its delicate point; that the gauze needed to make a single sponge for the general surgeon suffices to make half a dozen or more for the ophthalmic surgeon; that the solution in an eye-dropper is apt to be contaminated if the dropper is held with its tip uppermost; that a candle flame in a moderately darkened room, with the help of a convex lens, affords a far more satisfactory view of the eye than any amount of diffuse daylight, and that the proper place to hold the candle for such an examination is a little in front of, and fifteen or twenty inches distant from, the eye to be inspected.

She will also learn, or should learn, that the important point with reference to the illumination of a ward or room in an ophthalmic hospital is that it should be *constant*, that, for example, a window-shade should not be allowed to be blown back and forth by the wind, so that at one moment sunlight floods the room, and at the next moment it is comparatively dark; that a painful eye is often made less so by elevation of the patient's head with an extra pillow or two; that, especially after a delicate operation, a patient with both eyes closed should never be permitted to take a single step without guidance; that the easiest way to drop a solution into an eye, and the way least perturbing to a nervous patient, is to draw the lower lid slightly away from the eye, while the patient throws his head back and looks upward, and let the drop fall into the space between the lower lid and the eye; that, if it is important the solution should come, undiluted, in contact with the cornea, the upper lid should be drawn up and away from the eye, while the patient, with his head thrown back, looks downward, the cornea being thus exposed, so that the drop may be made to fall directly upon it; that in employing poisonous collyria, as, for example, a strong solution of atropine or hyoscyanine, it is best to instil into the eye one or, at most, two drops, while with non-toxic solutions it usually does no harm, though it is wasteful, to apply more than two or three drops; that an eye-dropper, if it is to be used for more than one patient, should not be contaminated by permitting its point to come in contact with the lid margin or eyelashes, and that a dropper with which atropine or other mydriatic has been instilled should not be used presently to apply, for example, a zinc or boracic acid solution to the eye of another patient, if one would avoid causing the second patient several days of unnecessary inconvenience from mydriasis. And, finally, if she is exceptionally clever and painstaking, the neophyte may, some day, succeed in making, with absorbent cotton and a wooden toothpick, a mop which, without reconstructing it and, further, without doing violence to his conscience, the surgeon can use.

One of the most responsible duties falling to the lot of a nurse in an ophthalmic hospital is the cleaning and sterilization of an eye preparatory to an important operation. In doing this she should be, in the first place, most careful that the antiseptic solution employed is of the prescribed strength, for, if it is too strong, marked conjunctival injection, if not actual inflammation, may be induced, necessitating, possibly—as has happened in my experience—a postponement of the operation; while, on the other hand, if it is too weak, the sterilization may be ineffectual. In the next place, while she should be thorough in washing the lids and in flushing the eye with the antiseptic, she should, at the same time, be gentle in her manipulations, bearing in mind that the eye is an organ that resents rough usage. This admonition, it may be observed, applies with equal force to her care of an inflammation of the eye attended by copious discharge, in which frequent cleansing is called for, as in gonorrhœal conjunctivitis. Here, it is of the greatest importance that, in removing the discharge, she should be most careful not to abrade the corneal epithelium, since such a seemingly trivial traumatism may be the starting point of a destructive secondary infection of the cornea. And, in this connection, it may be further suggested to the neophytic ophthalmic nurse, and, perhaps, to some who hardly deserve to be so classified, that in the management of infectious diseases of the eye a thorough washing of the hands with soap and water, after contamination, is a much safer and more effectual measure than simply dipping them for a moment, as I have seen practised, in a bichloride solution.

The Apothecary.—A few suggestions to the apothecary, which I should be glad to feel might be heeded, seem to be called for.

First, I would entreat him never to dispense a so-called "safety" eye-dropper, the kind that has a flange-like affair near the tip, since it is an unmitigated nuisance, and distinctly less safe than the ordinary dropper. Secondly, I would suggest to him never to furnish, with a collyrium, a straight-pointed eye-dropper nor one that has a sharply curved tip. The dropper that is most useful is one that is not too long and has a slightly bent and not too slender tip. It will, if necessary, draw the last drop of the solution from the vial, which the straight one will not do, and it is less likely to catch in the neck of the vial and be broken than is the one that is sharply curved. Thirdly, I would ask him to dispense the ophthalmologist's much-prescribed yellow oxide of mercury ointment not in an opal glass box, now so much in favor, but in an amber-colored one, since this prevents the chemical action of light upon the mercury salt, and preserves the ointment much longer.

Finally, I would beg him—and this I do with many misgivings, knowing how difficult it is to uproot an old prejudice—to lay aside the mortar and pestle in preparing solutions of

readily soluble drugs, such as sulphate of atropine, and, instead, simply put the ingredients in a clean vial, insert an equally clean cork, give the vial a shake, and be satisfied. If he knew, as I do, how much more apt the mortar and pestle solution is to develop a fungous growth, after standing a week or two, than the one prepared in the simple manner suggested, he would, perhaps, be "almost persuaded."

It has been a matter of no little astonishment to me to learn recently from one of the most reliable apothecaries in Baltimore, and also from the dean of the College of Pharmacy connected with the University of Maryland, that they still uphold and teach the propriety of using the mortar and pestle in the manner indicated, without reference to the solubility of the drug prescribed. Certainly, in these days of asepsis and antisepsis, and of warring against contamination, the practice seems distinctly anachronistic.

To the *surgical instrument maker* I would say: When one's favorite cataract or iridectomy knife is sent to be sharpened, pray use only an oil-stone if possible. Do not *grind* it, if it can be avoided; for, when the "favorite" comes home, after the grinding process, its owner too often can hardly look upon it without recalling, sadly, Byron's lines

> **Shrine of the mighty! can it be**
> **That this is all remains of thee?**

I would also call his attention to a reprehensible tendency, which in recent years seems to have possessed his craft, to make the shanks of such instruments as canaliculus knives and strabismus hooks inordinately long, and to another, equally reprehensible, tendency, to give too sharp a curve to the blades of iridectomy scissors and of iris forceps. And, in this connection, I would make the further suggestion that an iridectomy knife is more completely under the control of the operator, and can be used with more deftness, if the angle between the shank and the blade is very obtuse—considerably more so than is usually the case with those made at the present day.

The Manufacturing Optician I would intreat never again to furnish cylindrical glasses, *with opaque sides*, in an oculist's trial case. There is no possible advantage in making the cylinders in this fashion, and there are two decided disadvantages. In testing cylindro-prismatic glasses which one has prescribed it not infrequently happens that the opaque portion of the cylinder must be placed just where it obstructs one's view, and so prevents an accurate determination of the strength of the prism. Again, if the cylinder, especially with its axis approximately horizontal, happens not to be carefully centered in the trial frame, there will be complaint from the patient that something, probably the upper opaque portion of the lens, is obstructing *his* view.

The American Optical Company, and probably other manufacturing concerns, make cylinders with the axis marked by two small, circular, white discs placed about 2 mm. from the edge of the lens, and with a line, more exactly indicating the axis, running from each disc to the metal rim. I have found these most satisfactory, and, it seems to me, they can hardly be improved upon.

The only other suggestion I have to offer is to emphasize the great importance of accurately centering trial-case lenses. This is not always done with the exactness that it might be, and the consequence is that errors are liable to occur in one's estimate of ocular muscle faults, and, confusion and contradictory results in neutralizing compound prescription glasses in which there is a prismatic element.

NOTES ON NEW BOOKS.

Public Health Chemistry and Bacteriology. A Handbook for D. P. H. students. By David McKail, M. D. (Glasg.), D. P. H. (Camb.), etc. Price 6/6. (*New York: William Wood & Co, 1912.*)

The author is modest in presenting this work to the public. He claims for it no originality, and offers it merely as lecture notes compiled from various standard works. It is a small octavo of about 400 pages, the first 150 devoted to chemistry, the remainder to bacteriology. Under chemistry he discusses chemical and water analysis, examination of air, soils, foods, beverages, disinfectants, antiseptics and deodorants; under bacteriology general principles, results of bacterial activity, immunity and anaphylaxis, micrococci, non-sporing and sporing bacilli, spirilla, spirochætes, yeasts and moulds, and special bacteriological examinations. There is a constant demand for these elementary handbooks and this one may be recommended with safety to students, who will find it a simple and easy book from which to gain the first principles of the subject but nothing more.

Operative Obstetrics Including the Surgery of the Newborn. By Edward P. Davis, M. D. Illustrated. $5.50. (*Philadelphia and London: W. B. Saunders Company, 1911*).

This book covering nearly 500 pages clearly demonstrates that the obstetrician of to-day must be a competent surgeon. Concise descriptions of the well-known procedures to effect delivery are given, but the most valuable part of the text relates to the more recent innovations in operative obstetrics such as pubiotomy and vaginal Caesarean section. The author has taken the pains to collect the results of these operations as published to date. Those who advocate the operations have been quoted extensively but the various objections raised against them are also given. The advice offered with regard to their value is conservative, but no more so, perhaps, than is justified by the relatively short period of time in which there has been opportunity to test their usefulness and learn their limitations. It is disappointing to find the lateral posture recommended for the performance of forceps operations. The practical character of the book will increase its popularity; the illustrations, of which there are 264, will prove most helpful to those who have not had the opportunity to witness the performance of the operations. It is a hopeful sign of progress in American text-books to find bibliographies, such as are here given; they are certain to stimulate students and practitioners to consult original sources.

Oxford Medical Publications: Common Disorders and Diseases of Childhood. By George Frederick Still, M. A., M. D., etc. Second edition. $5.50. (*London: Henry Frowde and Hodder & Stroughton, 1912*).

The new appearance of this book only increases our appreciation of it, which was expressed in our issue of December, 1911. The author has written an excellent work; he does not, as his

title indicates, endeavor to cover *all* the diseases of children, but only the commoner ones with which he has had a large experience, and these are the ones that the general practitioner meets with and wants to know how to treat. If he studies Still's work, he will be well guided. We wish that other authors would follow in Still's footsteps, and write rather on the diseases they are constantly seeing than on diseases which are practically unknown to them. Many of the treatises on medicine, surgery, etc., are poor because the authors attempt too much, not having had the necessary experience to write comprehensive works. The modifications of this second edition add to its value, and we commend the work heartily once again to the medical profession.

BOOKS RECEIVED.

The Treatment of Shortsight. By Prof. Dr. J. Hirschberg. Translated by G. Lindsay Johnson, M. D., F. R. C. S. With twelve illustrations. [1912.] 12°. 123 pages. Rebman Company, New York.

A Textbook of Ophthalmology. In the Form of Clinical Lectures. By Dr. Paul Roemer. Translated by Dr. Matthias Lanckton Foster. With one hundred and eighty-six illustrations in the text and thirteen colored plates. Volume I. [1912.] 4to. 275 pages. Rebman Company, New York.

Fourth Report of the Wellcome Tropical Research Laboratories at the Gordon Memorial College, Khartoum. Volume B.—General Science. Andrew Balfour, M. D., B. Sc., F. R. C. P. Edin., D. P. H. Camb., Director. 1911. 4to. 333 pages. Published for Department of Education, Sudan Government, Khartoum, by Baillière, Tindall & Cox, London; Toga Publishing Company, New York.

A Surgical Treatment of Locomotor Ataxia. By L. N. Denslow, M. D. 1912. 12mo. 118 pages. Baillière, Tindall and Cox, London.

United States. Treasury Department. Public Health and Marine Hospital Service. Annual Report of the Surgeon General of the Public Health and Marine Hospital Service of the United States. For the Fiscal Year 1911. 8vo. 331 pages. 1912. Government Printing Office, Washington.

Immunity. Methods of Diagnosis and Therapy and their Practical Application. By Dr. Julius Citron. Translated from the German and edited by A. L. Garbat. Twenty-seven illustrations, two colored plates and eight charts. 1912. 8vo. 209 pages. P. Blakiston's Son & Co., Philadelphia.

La Vie et les Maladies du Sang. Par le Dr. G. Froin. 1911. 8vo. 240 pages. G. Steinheil, Paris.

Les Otites Moyennes et Leurs Complications. Par Pierre Descomps et Paul Gibert. Avec une préface de P. Sebileau. 1912. 8vo. 256 pages. G. Steinheil, Paris.

Transactions of the College of Physicians of Philadelphia. Third Series. Volume the Thirty-third. 1911. 8vo. 416 pages. Printed for the College, Philadelphia.

A Cyclopedia of American Medical Biography. Comprising the Lives of Eminent Deceased Physicians and Surgeons from 1610 to 1910. By Howard A. Kelly, M. D. Illustrated with Portraits. Two Volumes. 1912. 8vo. W. B. Saunders Company, Philadelphia and London.

State Board of Health of the State of Ohio. Twenty-fifth Annual Report for the Year Ending December 31, 1910. 8vo. 410 pages. 1911. Columbus, Ohio.

National Association for the Study and Education of Exceptional Children. Proceedings of the Second Annual Conference on the Problem of the Exceptional Child. December 1-2, 1911. 8vo. 190 pages. Richard G. Badger, Boston, Mass.

Kystes Hydatiques du Poumon. Par Pedro Escudero. 1912. 8vo. 270 pages. G. Steinheil, Paris.

An Index of Differential Diagnosis of Main Symptoms. By Various Writers. Edited by Herbert French, M. A., M. D., Oxon., F. R. C. P., Lond. With sixteen colored plates and over two hundred illustrations in the text. 1912. 8vo. 1017 pages. John Wright & Sons, Ltd., Bristol; Simpkin, Marshall, Hamilton, Kent & Co., Ltd., William Wood & Co., New York.

The Medical Annual. A Year Book of Treatment and Practitioner's Index. Thirtieth Year. 1912. 8vo. 887 pages. John Wright & Sons, Ltd., Bristol; Simpkin, Marshall, Hamilton, Kent & Co., Ltd., London.

The Prevention of Dental Caries. By J. Sim Wallace, D. Sc., M. D., L. D. S. Second edition. 1912. 8vo. 67 pages. Office of the Dental Record, London.

Surgery of Deformities of the Face, Including Cleft Palate. By John B. Roberts, A. M., M. D. Illustrated with 273 figures. 1912. 8vo. 273 pages. William Wood & Company, New York.

Diagnose und Therapie der Magen- und Darmkrankheiten. Anhang: Die chemische und mikroskopische Untersuchung des Mageninhaltes und der Fæces. Von Privatdozenten Dr. Walter Zweig. Zweite, vermehrte Auflage. Mit 36 Textabbildungen und 1 farbigen Tafel. 1912. 4to. 502 pages. Urban & Schwarzenberg, Berlin & Wien; Rebman Company, New York.

Nervöse Angstzustände und ihre Behandlung. Von Dr. Wilhelm Stekel. Mit einem Vorwort von Professor Dr. Siegmund Freud. Zweite, vermehrte und verbesserte Auflage. 1912 4to. 448 pages. Urban & Schwarzenberg, Berlin & Wien; Rebman Company, New York.

On Bronchial Asthma. Its Pathology and Treatment. By J. B. Berkart, M. D. Revised and abridged third edition. 1911. 8vo. 150 pages. Henry Frowde, Oxford University Press, London, Edinburgh, New York, Toronto and Melbourne.

Lateral Curvature of the Spine and Round Shoulders. By Robert W. Lovett, M. D. Second edition, revised and enlarged with 171 illustrations. 1912. 8vo. 192 pages. P. Blackiston's Son & Co., Philadelphia.

A Manual of Surgical Treatment. By Sir W. Watson Cheyne, Bart., C. B., D. Sc., LL. D., F. R. C. S., F. R. S. and F. F. Burghard, M. S. (Lond.), F. R. C. S. New Edition. Entirely revised and largely rewritten with the assistance of T. P. Legg, M. S. (Lond.), F. R. C. S. and Arthur Edmunds, M. S. (Lond.), F. R. C. S. In Five Volumes. Volume II. 1912. 8vo. 570 pages. Lea & Febiger, Philadelphia and New York.

The Ocular Muscles. A Practical Handbook on the Muscular Anomalies of the Eye. By Howard F. Hansell, A. M., M. D., and Wendell Reber, M. D. Second edition, rewritten, enlarged. With 3 plates and 82 other illustrations. 1912. 8vo. 223 pages. P. Blackiston's Son & Co., Philadelphia.

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